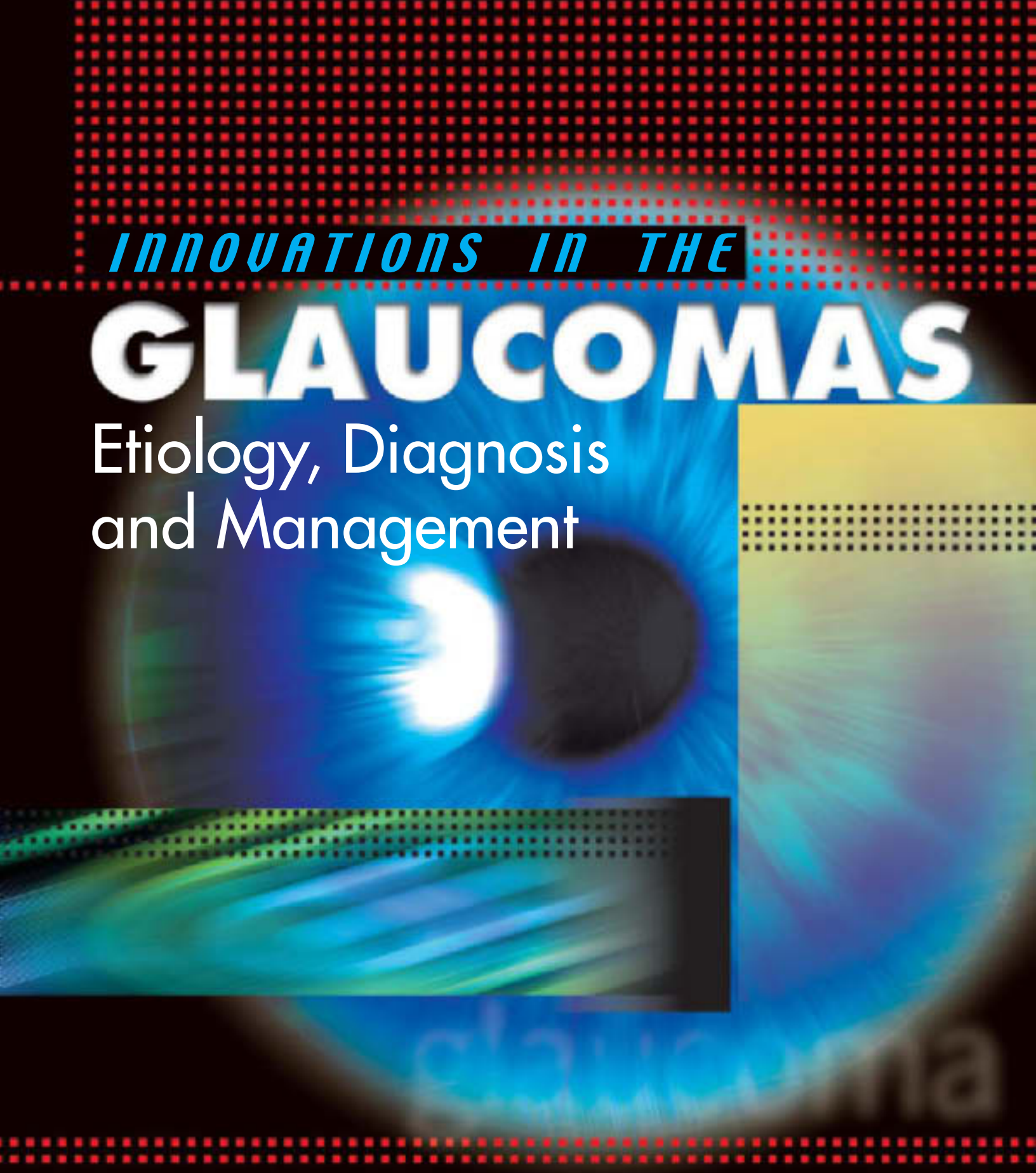


INNOVATIONS IN THE GLAUCOMAS

Etiology, Diagnosis and Management

HIGHLIGHTS OF OPHTHALMOLOGY
INTERNATIONAL

Editors:
Benjamin F. Boyd, M.D., F.A.C.S.
Prof. Maurice Luntz, M.D., F.A.C.S.
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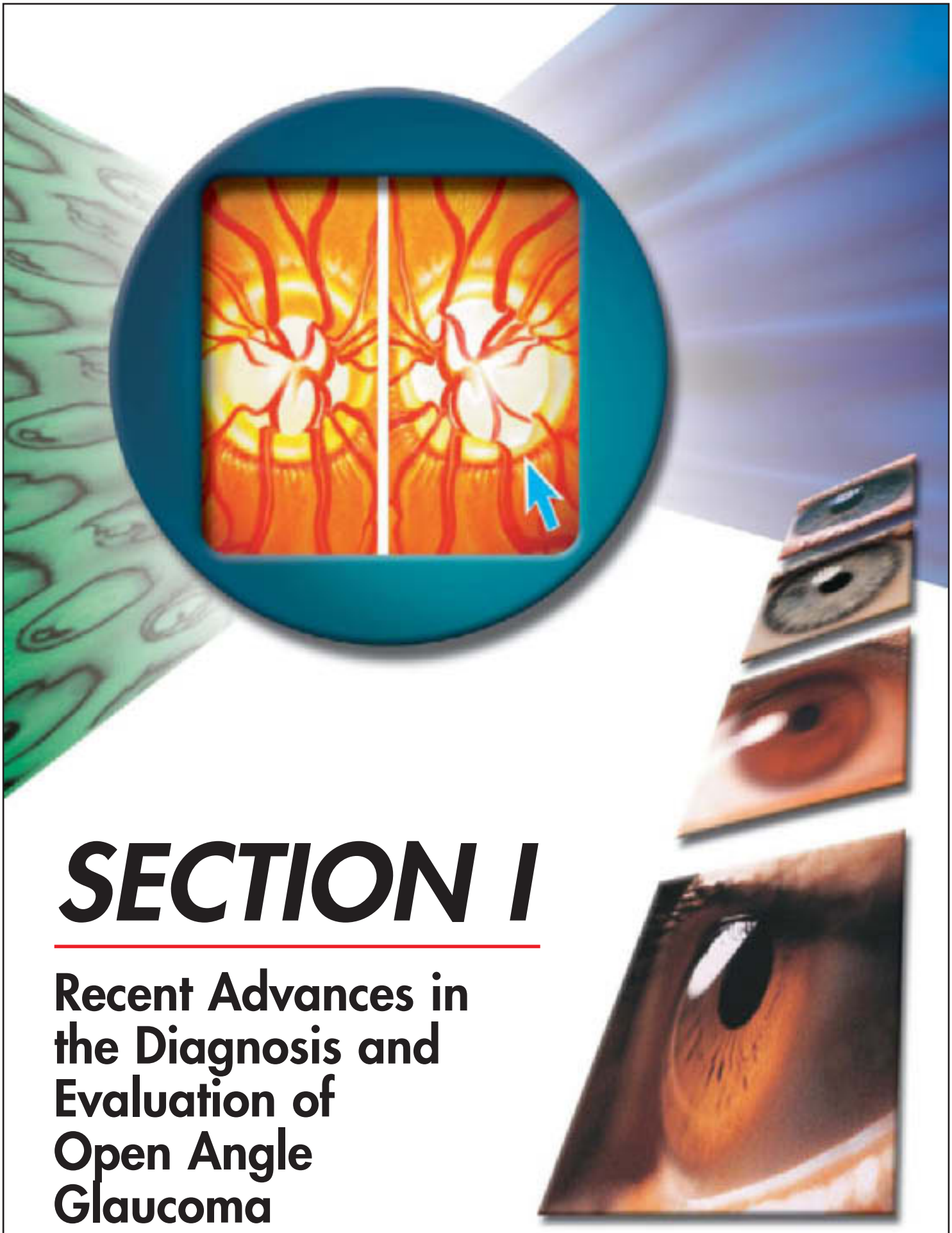
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SECTION I

Recent Advances in the Diagnosis and Evaluation of Open Angle Glaucoma

Chapter 1
OPEN ANGLE GLAUCOMA

Benjamin F. Boyd, M.D., F.A.C.S.
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CLINICAL EVALUATION AND RISK FACTORS

Significant Advances in Early Diagnosis

In addition to the progress brought on in the last few years by automated visual field testing (Figs. 1 and 2), there are three outstanding features that have proven to be a significant step forward in the early diagnosis of glaucoma.[1,2] These features are: 1) Improvements in detecting the actual changes in the optic disc related to glaucoma (Fig. 3); 2) [3] the detection of changes in the nerve fiber layer which point to the diagnosis of glaucoma before the onset of visual field loss; [3] 3) a better understanding of the relationship between intraocular pressure and glaucoma and the risk factors that predispose to the actual development of glaucoma.[2]

Quigley has emphasized that the best methods for detecting early damage in glaucoma at the present time involve examination of the disc (Fig. 3) and the nerve fiber layer and conducting an automated visual field test (Figs. 1, 2).[4,5]

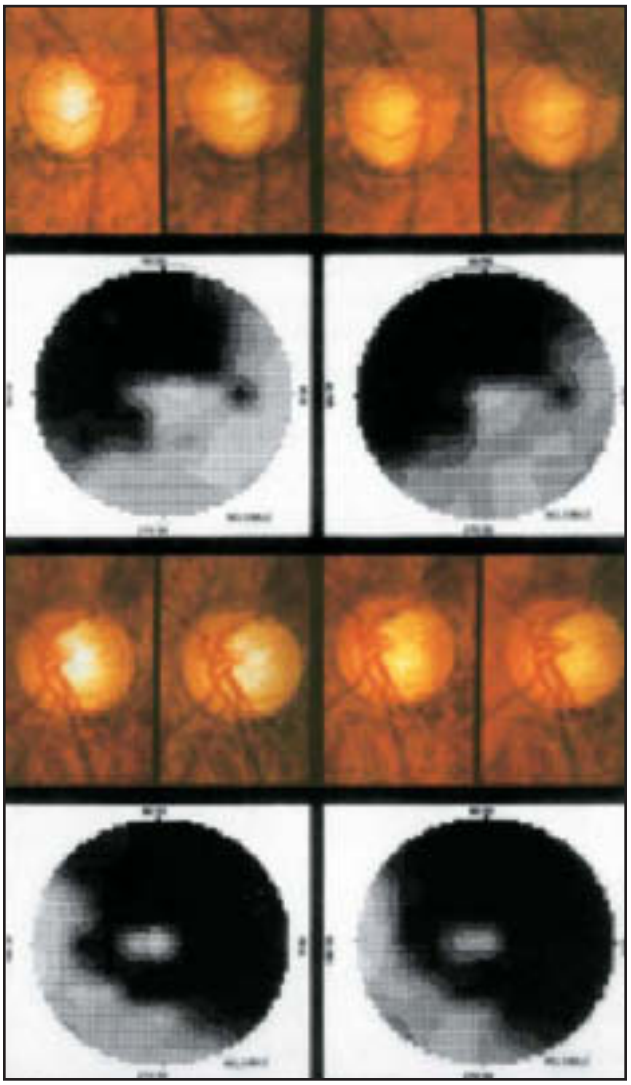


Fig. 1: Comparative Stereophotographs of Optic Discs and Corresponding Computerized Visual Fields.

Figure 1 shows a laminated card which ideally is given to the patient and sent to his/her ophthalmologist. It incorporates stereophotographs of the optic nerves of both eyes and the corresponding computerized visual fiels side by side but taken at different dates. This allows the physician to make a comparative analysis of any change instantly. Additional information of significance accompanies this card. It always contains baseline data such as intraocular pressure from the initial visit and comparative data from the visit preceding the current visit, so that near term comparison can easily be made. This very practical system was initiated by Dr. Ken Richardson at the Glaucoma Laboratory at Baylor College of Medicine.

The Significance of Intraocular Pressure

All of us as clinicians are absolutely right in being concerned about patients who have a higher intraocular pressure. **Alfred Sommer,** based on extensive epidemiological studies done at the Wilmer Institute, Johns Hopkins Hospital, Baltimore, emphasizes that there really is no such thing as a normal pressure and an abnormal pressure.(6) The intraocular pressure figures that are used to determine whether the pressure is "normal" or "abnormal" are simply a statistical technique that divides the distribution of pressures in the normal population. They say nothing about what is abnormal in a specific patient.

What we know is that the higher the intraocular pressure, the greater the risk that the patient will develop glaucomatous optic nerve damage. So, if the patient has a pressure of 18 for example, his/her risk of developing glaucomatous optic nerve damage is lower than if the pressure is 28. But that does not mean that somebody with a pressure of 28 will definitely develop glaucoma because they may not; nor does it mean that someone with a pressure of 18 will never develop glaucoma because they may.

The level of IOP needs to be considered with the appearance of the cup to disc ration of the optic nerve head. An eye with a C:D > 0.5 is at higher risk of developing glaucoma and visual field loss. The higher IOP the greater the risk. The larger the C:D the higher the risk of developing glaucomatous visual field loss.

Sommer considers that pressure is really a risk factor that tells us we should be more suspicious and concerned about an individual the higher his/her pressure may be.(7) This concern should lead us to get a baseline visual field test and probably see them back again in 6 or 12 months to reassure ourselves that they are not suffering damage to their optic nerve. As we see them back and become increasingly reassured that their optic nerve is remaining normal, then we would see them fewer and fewer times. If, however, there is increased evidence that there is damage to their optic nerve, we would see them more frequently until we are certain that there is damage and then, of course, we would treat them adequately.

Intraocular pressure is the major but not decisive risk factor in the early disease process. Patients who have a pressure that is lower than 18 or 20, are at less risk of developing glaucomatous optic nerve damage. If their optic nerve looks at all abnormal in C:D > 0.6 or vertical elongation of the C:D, however, we should do a visual field test and if that is suspicious we would see them back again in a few months to re-examine and re-test them. At this stage a SWAP (Short Wave Automative Perimetry) visual field should be done.

Can We Exclude Glaucoma on the Basis of Intraocular Pressure?

Based on **Al Sommer's** studies, half of the people who have visible glaucomatous optic nerve damage and a visual field defect that is typical for glaucomatous optic nerve injury, will have a pressure that is less than 22 at the first examination. Therefore, we cannot exclude glaucoma on the basis of intraocular pressure only(6).

Intraocular Pressure Levels - An Arbitrary Division

Let's discuss the controversial question of ocular hypertension. **Sommer**(7) thinks that we made a big mistake in the past. Because we had "magic numbers": above a pressure of 21 is abnormal and below a pressure of 21 is normal, we artificially divided all patients into more groups than made sense. The most important attribute of glaucoma is the status of the optic nerve. If we give it the importance it deserves, we should have two groups of people: those who are normal because their optic nerve looks normal and is functionally normal when you test the visual field, and those people who have glaucomatous abnormalities and therefore have glaucoma. They have an abnormal optic nerve and it is abnormal either in its appearance (Fig. 3) or evidenced by the presence of a characteristic visual field defect (Figs. 1 and 2).

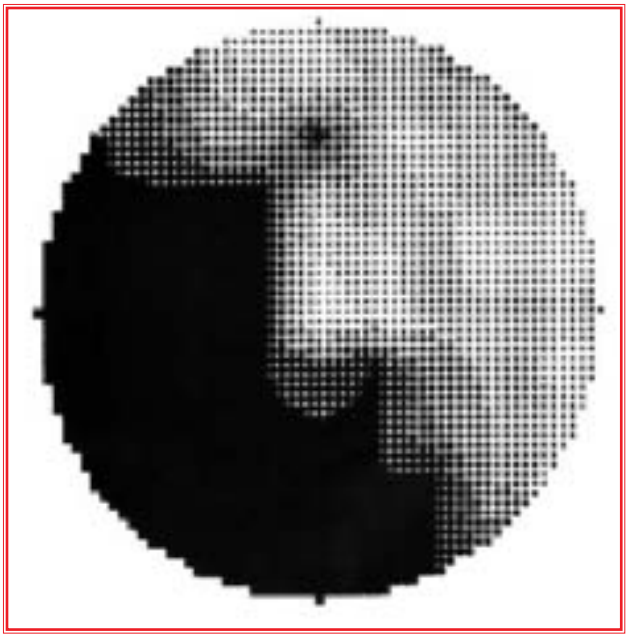


Fig. 2: Automated Computerized Visual Fields.

Visual fields as shown in Fig. 2 can be made with computerized automated equipment such as the Humphrey Analyzer or the Octopus. This figure demonstrates advanced glaucoma loss in the right eye with a residual central and temporal island. The greatest sensitivity of the retina is represented in white with incrementally darkening gray used to illustrate respectively decreased retinal sensitivity. Areas of absolute loss of retinal function are black.

By including intraocular pressure in the definition and arbitrarily saying that IOP greater than 21 is abnormal, we have made four groups out of two groups: two of the groups have optic nerves that appear to be entirely normal, one with a pressure that is below 21 which we call "normal", and one with a pressure above 21 which we call ocular hypertension. On the other hand, with people whose optic nerves are abnormal we have divided them arbitrarily into two groups: there are those whose optic nerves are abnormal and their pressure is above 21 and we make the diagnosis of glaucoma. And then we have people who have the same abnormality of the optic nerve but their pressures are 18 or below and we say these people have "low tension glaucoma".

In "low tension glaucoma" ischemia of the optic nerve head probably plays the major role and IOL is of secondary importance. Nevertheless, reducing IOP in these eyes does slow the progression of the disease. Localized ocular vasospasm may play a part and many of these patients have migraine or Raynaud's disease. A significant number of these patients have previously had glaucoma secondary to uveitis or to steroid therapy, primary open angle glaucoma masked by oral beta-adrenergic antagonists, or may suffer from diseases that damage the optic nerve such as intracranial tumors, carotid obstruction or syphilis.

Improving Our Understanding of the Relation Between Pressure and Glaucoma

We must improve our understanding of the relation between pressure and glaucoma. Although the most significant risk factor for the development of glaucomatous damage is elevated intraocular pressure, even elevated intraocular pressure, however, may be misleading and may not indicate glaucoma. 25 percent of normal people over 65 have intraocular pressure of 20 mm Hg or higher. "Ocular hypertension" of 21 mm Hg or above occurs in an estimated 7-10% of the general population.

We do not have any way of determining objectively the level of safe limit of pressure for an individual eye unless the patient shows optic disc changes and visual field loss from a specific intraocular pressure. Really, 16 mm Hg is the average pressure in the majority of normal subjects. The level of 21 mm Hg is a statistical figure considered to be a "two standard deviation" of the mean average which is 16 mm Hg. If 16 mm Hg is the mean of the normal population, a diseased eye should have a level closer to that pressure with any mode of treatment. **S. Nagasubramanian, M.D.**,[8] from the Glaucoma Service at Moorfields Eye Hospital in London has studied this problem for 20 years. He considers that as the statistical approach would have 21 mm Hg as the upper limit of normal, we should not assume that 21 mm Hg is going to be the safe limit for established cases of open angle glaucoma.

The well established risk factors (family history, myopia, diabetes, black race, age and trauma) are fundamental in orienting the clinician toward the proper diagnosis.

Very Early Signs - The Comprehensive Eye Examination

How can the clinician determine who is going to develop glaucoma and who is not remains a difficult problem. A comprehensive eye examination and a good history searching for risk factors is absolutely mandatory.

Importance of Risk Factors

We have the intraocular pressure as a starting point. Quigley[4] strongly advocates measuring the patient's pressure multiple times and at different times of the day to determine that particular person's average pressure. We also have the history that will give us clues to risk factors. Do they have a family history of glaucoma? If other members of the family have had glaucoma, and especially if they have gone blind from glaucoma, then that makes us more suspicious. There may also be people who develop secondary glaucoma because they have had trauma to their eye. And people who have myopia. That is another well-established risk factor. The same is true for diabetes, black race and the age of the patient. Blacks have a much higher incidence of open angle glaucoma than whites.

Clues from Optic Nerve Examination

We must look very carefully at the optic nerve. There are specific signs suspicious of glaucoma. One is that the cup is larger than usual (3A). Although the term "cup" is not quite descriptive enough, it is generally agreed that we refer to the empty space in the middle of the optic disc which in glaucoma increases and finally becomes excavated. If the cup is symmetrically larger than a cup to disc ration of 0.6 which is the bimodal curve for the normal population or if it is vertically elongated so it is taller than it is wide, or if it is notched, if the neuroretinal rim is very thin, very often at the seven o'clock and five o'clock positions in relationship to the temporal side of the disc, then that raises the suspicion that in fact, there is damage to that optic nerve (Fig. 3 B). If we compare the patient's two eyes, we often find that one eye is losing fibers faster and has more damage than the other. Consequently, the usual symmetry in cup size and disc size becomes asymmetric. So we are looking, then, for asymmetry associated with excavation either within the disc itself at the 12 and 5 or 7 o'clock positions or between the right eye and the left eye.

Certainly, if we see a disc hemorrhage, this constitutes a significant finding. That does not occur very frequently in glaucoma, but when it does occur, it signifies an infarct and is evidence that the wall of the optic nerve at that point is collapsing. The optic nerve is atrophying. The optic disc finding of glaucoma is a loss of disc rim tissue manifesting as an enlargement of the cup associated with a deeper floor and an undermined or excavated rim (Figs. 3 B and 4). The loss of disc rim tissue is sometimes relatively greater at the upper and lower disc poles, the 6 and 12 o'clock positions.

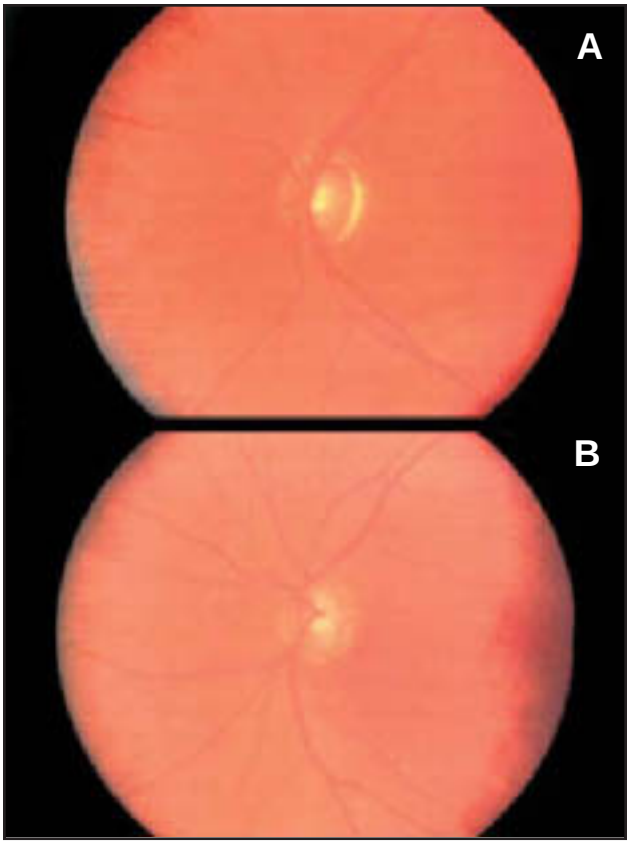


Fig. 3: Clues from Optic Nerve Examination - Normal and Abnormal Cups

Fig 3 (A): Patient with elevated intraocular pressure but normal visual field, displays an oval disc, but not an abnormally oval cup. The cup is small, with nice, thick pink disc rim for 360 degrees. Fig 3 (B): Shows early optic nerve damage, superior visual field defect and inferior nerve fiber loss. Note the cup is narrow but clearly vertically enlongated, and the disc rim is very thin inferiorly.

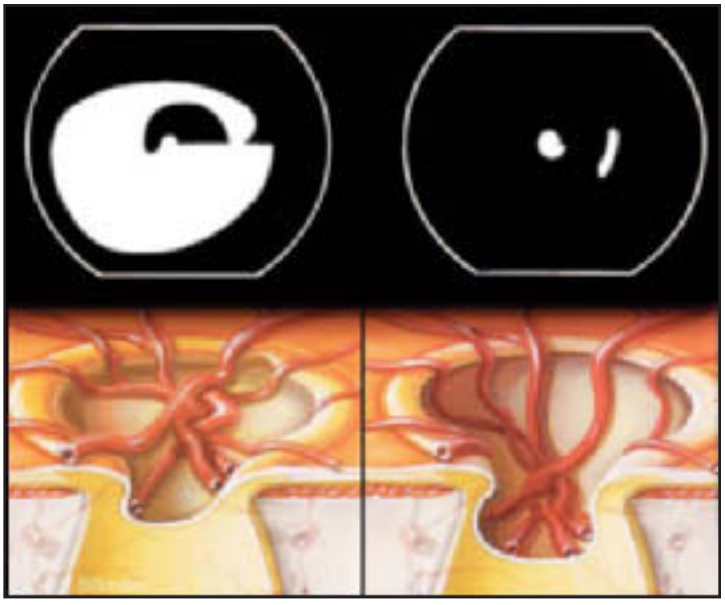


Fig. 4: Advanced (left) and Far Advanced (right) Glaucomatous Cupping

These figures show that as tissue is lost from the optic nerve head in advanced (left) and far advanced (right) glaucoma the overall structure moves backward physically. Quigley describes this as the rim actually rotating out underneath its own margin so that it looks as if one could put one's finger in under the rim. This is what we refer to as excavation. It is quite uncommon in any disease other than glaucoma for the surface of the disc to recede dramatically from the surface of the retina. In this case the cup floor goes backward much more rapidly, and this excavation almost looks as if it has a sharp edge. This particular feature happens in glaucoma and almost nothing else.

Importance of Visual Fields Testing

Once we become suspicious that there is damage to the optic nerve because of the appearance of the disc, then we should certainly do a very good, rigorous visual field examination for present and future reference. Visual field loss in chronic open angle glaucoma is thought to be a combination of diffuse and local dropout of nerve fibers at the optic nerve head, leading to diffuse or localized visual field defects.

While the development of automated perimetry has significantly improved visual field testing, the most significant improvement in glaucoma evaluation may be the more widespread use of automated visual field testing. Evidence is increasing to show that the high quality instruments used for automated perimetry are able to detect abnormalities earlier than manual perimetry. They also produce results that are difficult to interpret. Our present challenge is to sort out which of the apparent abnormalities detected by the new tests are truly defects due to glaucoma and which are false positives (Figs. 1 and 2).

Only a few years ago we did visual field testing on a much more selective basis because it was very time consuming and competent field technicians were difficult to find. Now, nearly every ophthalmologist's office can accurately test the patient's visual field in a cost-efficient fashion. The new field testing is more sensitive in detecting glaucoma at an earlier stage. In cases of advanced glaucoma with severe visual field loss, automated perimetry may become tiring in some older patients. Goldmann visual field testing with a technician in attendance is preferable in these patients.

Selective Damage Undetected by Conventional Perimetry

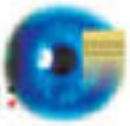
Studies done at the Wilmer Institute with automated perimetry have revealed that, among glaucoma suspects who do not have abnormalities in the Goldmann field test, a sub-population exists in whom damage has already occurred before that stage we formerly called Goldmann field loss. In this subgroup, which may represent as many as 20 or 30 percent of suspects, glaucoma can now be detected with much greater accuracy and reproducibility through automated field testing. The loss of retinal neurons could amount to between 25% to 40% before we can establish any functional loss with conventional perimetry. **Nagasubramanian**(3) points up that, based on the work by **Quigley**(4) and other recent studies, there may be large diameter optic nerve fibers which may be selectively damaged in the early stages of the disease. These fibers account for about 5-10% of all optic nerve fibers, so the loss is considerable. Conventional perimetry does not specifically look for changes in the function of these ganglion cells, which may explain why we have been unable to pick up very early functional changes even in eyes with large, suspicious looking cups with high pressures.

The automated visual field needs to be repeated two or three times over a six month period to establish a baseline for the visual fields. There is an element of learning effect in the first few weeks if not few months and patients have to become familiar with the particular system to which they are subjected to.

Natural History Between High IOP and Visual Field Loss

In spite of inconsistencies regarding intraocular pressure, the natural history of high intraocular pressure is field loss. There is a long interval between the onset of increased intraocular pressure and the development of visual field loss and even longer until there is measurable loss of visual function. Untreated patients with intraocular pressure between 21-30 mm Hg have seven times greater incidence of field loss after 20 years follow-up than patients with normal pressure.

The automated visual field test is still a subjective test and subject to variability of responses by



the patient. More objective tests are being developed (see chapters on "Advances in Visual Field Testing," "Optical Coherence Tomography," and "Retinal Tomography" - Chapters 4 and 5).

Genetic research of glaucoma is adding another method of recognizing patients at risk of developing glaucoma or with early glaucoma.

TARGET PRESSURE LEVEL GOALS

One of the most important developments in the management of glaucoma is a general principle on the goals to be attained regarding pressure levels. The experts who see many patients with glaucoma, and ophthalmologists in general, are coming to recognize that our previous conception of what is good control was somewhat oversimplified. We now recognize that we probably need to be more aggressive in our therapeutic approach to patients, particularly with more advanced glaucomas. In patients with a 0.9 cup to disc ratio, most ophthalmologists used to think that a pressure of 20 mmHg was acceptable. Most of us would agree today that in somebody with a very large cup, a pressure of 20 mmHg is too high, and that we need to get a lower pressure.

The American Academy of Ophthalmology's "Preferred Practice Pattern for Glaucoma" coins the term **"Target Pressure"**. Target pressure is a pressure which you think will save the optic nerve in a particular patient. When you first see the patient, and his/her pressure is 24, you may think that 19 is a good "target pressure". But even if you get the pressure to 19 you must continue seeing him/her regularly and monitor the optic nerve. Anything that would suggest the optic nerve has become worse, either the appearance of the optic disc or the nerve fiber layer, or the function of the optic nerve as measured by the visual field, retinal tomography or optical coherence tomography[3]: if any of these gets worse, then the chosen target pressure is wrong. If you had picked a target pressure of 19, that is not adequate. This person needs a target pressure of maybe 16. Or maybe this person needs a target pressure of 12. But you keep adjusting the target pressure until you stop the deterioration of the optic nerve; you do not relax simply because you have a pressure that is below 21. The main reason why patients continue to lose visual fields is that the treatment they are using is leading to suboptimal lowering of intraocular pressure, or unrecognized spikes of IOP.

When Can Treatment Give a False Sense of Security

We would do much better if we forget the arbitrary divisions of IOP and simply recognize the fact that when the pressure is higher we have a higher risk of having glaucomatous neuropathy but we can have glaucoma at quite low pressures. That is very important for diagnosis but it is even more important for treatment. If you can get glaucomatous optic nerve damage at any pressure, simply because a patient comes to you with a pressure of 24 with glaucomatous optic nerve damage and you lower the pressure to 20 with medicines or with laser or with filtering surgery, it does not mean you have controlled the disease. Often, with a pressure of 20 mm Hg, the clinicians feel they have cured the patient, when they may not have helped him/her sufficiently. It may be that the pressure has to be lowered to 16 to protect the optic nerve from further damage. Too many clinicians get a false sense of security by evaluating results essentially on intraocular pressure levels and keeping the patients on suboptimal pressure levels.

It is also important to keep in mind that in a chronic disease, resistance is more likely to gradually decline with time and the patient who develops glaucoma damage is probably an individual who either has a gradually elevating pressure or pressure spikes or a gradually declining resistance to the level of his/her IOP with time or both. This not only refers to those in the population who will develop glaucoma damage, but also to those who have glaucoma damage and who are more likely to develop an increasing amount unless they are maintained under a tighter control than would usually be considered necessary.

The Role of Maximum Medical Therapy

One of the most important advances in medical therapy is an increasing consensus that if maximum medical therapy combining the three basic topical medications (betablockers, alpha adrenergic agonists or prostaglandin analogs) plus oral or topical carbonic anhydrase inhibitors is necessary to achieve target pressure control then control of the glaucoma will not be well maintained. Most of these patients have borderline in-traocular pressures and it is precisely at this stage that they continue to lose visual fields. Instead of leaving a patient on maximum medical therapy, he/she should be treated with laser trabeculoplasty or surgery.

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Chapter 2
OVERVIEW OF CLINICAL DIAGNOSTIC PARAMETERS FOR GLAUCOMA

Alan S. Crandall, M.D.

Evaluation of Suspected Glaucoma

Several objective methods are used to evaluate when patients in whom glaucoma is suspected should be considered cases of true glaucoma, or when glaucoma can be ruled out. It is easier to rule glaucoma in that out, because even the newer objective methods still require almost a 40% loss of tissue before the presence of disease can be documented. A good binocular evaluation of the disc by an experienced ophthalmologist is the most important method for identifying the presence of glaucoma. This evaluation can be supplemented with monocular evaluation, (direct ophthalmoscope – Editor) stereo photographs, visual fields, and then the newer technologies of retinal topography. Closely documenting all findings is essential in order to follow changes related to glaucoma over time.

Binocular and Monocular Evaluation

A dilated stereoscopic view of the disc is the best way to evaluate potential changes in a patient in whom glaucoma is suspected, using a 78 diopter lens at the slit lamp for binocular evaluation. As trained using monocular views, we tend to look at the disc monocularly first and then to translate that image into a stereoscopic view for evaluation. Critical findings can be missed unless patients are examined monocularly and then dilated for binocular assessment. In addition to white light, green or red free light should be used to look not only at the disc margins but also at the nerve fiber layer to determine dropout and to evaluate the health of the tissues as they leave the disc.

Evaluation of the Disc

We look first at the overall shape of the disc, at the scleral tissue and try to assess whether there is a myopic crescent and whether there are pigment changes that might affect color. Look at the choroid surrounding the area, and determine whether the disc slopes or whether the margins are crisp. Then we look at the nerve fiber layer pattern in each of the quadrants. The first areas that tend to drop out are superiorly and inferiorly at the temporal rim.

In conducting these evaluations, it is very important to understand the size of the eye and its refractive error. For instance, a fairly large cup-to-disc-ratio is very significant in a patient with five diopters of hyperopia, but the same ratio would cause less concern in a patient with -5 diopters of myopia. The volume of nerve fiber layer in the scleral rim in a +5 hyperope is likely to be less than the potential volume in a person with myopia. The scleral rim will be quite large in the myopic eye, and the fibers will have space to spread out naturally, whereas in a hyperopic eye all the volume of the nerve fiber layer is confined in a relatively small space. The ability to see down to the cribiform plate in a hyperopic eye is a disturbing finding. It means that some loss of nerve fiber tissue has occurred in that eye.

Assessment of Vasculature

Evaluation of the peridisc capillaries leads to an assessment of the architecture of all the arteries and veins. Check whether the arteries and veins form a normal branching pattern or whether there is something unusual in the branching pattern or in the ratio of arteries to veins. Visualize the entire structure carefully so that changes on subsequent examinations can be recognized. Evaluation of these patterns is made easier by some of the newer dark adaptive lenses. These lenses facilitate an examination of color change, areas of capillary dropout, and changes in the width of the neural rim.

Look for several aspects of the vasculature in each of the four quadrants. One of the most important questions to answer is whether the vessel pattern appears to go under the rim of the neural disc margin or through it. This is especially important in order to detect change over time. As nerve fiber layer dropout begins to occur, the vessels will go under the disc outer rim margin. This is a very important sign of glaucoma change. Assess whether any change has occurred in the pattern of the vasculature as it goes around the inner rim of the neural disc. There appears to be a relationship between vessel shifting and the volume of the cup itself.

To assess the cup-to-disc ratio first estimate the total scleral rim diameter. Looking at the superior quadrant, from superior to inferior, attempt to find the distinct disc outer rim margin. From this rim of the neural tissue, move to the point that is the inner rim of that tissue. This distance might appear to be 0.2 to 0.4 of the overall diameter. Evaluate the degree of pallor in each of the quadrants because it relates not only to disc change but also to the potential for visual field changes. Psychophysical testing can then be done to document the patient's status.

Documentation of the Optic Disc Examination

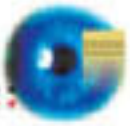
Document the structure of the disc very carefully, with drawings, serial photographs, and a written description of exactly what has been noted in each quadrant in order to determine whether change has occurred on future examinations. The neural rim is described individually. Note whether it looks the same in each quadrant or whether it is narrower in some places than others. Compare the neural rim tissue in each quadrant with that in the other quadrants by color, margins, and shape. Accurately describe and draw the cup-to-disc ratio. Indicate whether any sloping is present. Note also vessel displacement, measurements of the vessels, the volume of the disc, and the depth of the cup.

In contrast with other techniques, we use charts divided like the quadrant of a clock, to try to reflect exactly what is seen in each of the four quadrants. We use colored pencils to draw how the disc appears. Obviously, the chart has limitations in that it attempts to represent three-dimensional quadrants in a single plane. Indicate the pattern of nerve fibers in each quadrant because that is where dropout will later be visible, particularly in the superior and inferior margins. For example, if it is documented that the right eye superior quadrant has no area of nerve fiber layer dropout and has good crisp disc margin then looking at this drawing the following year and at the superior nerve fibre layer it should be possible to recognize if there has been some area of nerve fiber layer dropout in the superior quadrant.

Visual Fields

Follow this clinical evaluation of the disc, with a visual field assessment, for which we use the Fast Pack 32. (An alternative is the 24-2 SITA FAST – Editor). Some of the most difficult discs are the -4, -5, -6, and -7 diopter myopes that already have a myopic crescent.

We use both the Humphrey package and an Octopus package, but prefers the Humphrey package. In using automated visual fields, it is important to keep in mind that the patient must undergo a period of learning with this technology, and fatigue of the patient can be an important factor. (In this respect the SITA FAST strategy is useful – Editor). The first automated visual field is often relatively incorrect.



The ophthalmologist must sit down with the patient and explain how the evaluation works. We should explain that it is not really a test in order to help relieve anxiety and to encourage the patient to participate in a more relaxed fashion.

Although the ophthalmologist certainly cannot assess change over time on the first occasion he sees a patient, establishing a baseline for future reference is critical. On a yearly basis or every 2 years, we repeat visual fields and compare them with previous visual fields. There is not yet a clear answer to the question of how frequently visual fields should be tested. How readily changes associated with glaucoma can be picked up from changes in the visual fields is currently being assessed. Progression can probably be picked up more readily with the current visual field results before it can be identified through examination on the optic nerve.

Stereoscopic Photographs

Serial stereoscopic photographs are done every 2 to 3 years. These are placed in the patient's chart for comparison. Either immediately before or immediately after the patient's visit the previous photographs are viewed using a stereoviewer in the office. A reticle that can be placed on the disc improves the accuracy of comparing photographs. Additionally, red free photographs are used to assess the nerve fiber layer. Awareness of other changes in the patient, for instance the development of cataracts, is important as these changes would obviously diminish the ability of the photographer to capture useful images.

The current literature suggests that the SWAP (Short Wavelength Automated Perimetry) may help in earlier identification of defects related to glaucoma. In our busy practice, we have not found it as helpful as SITA in identifying defects. The challenge is that many patients have other defects such as cataracts and macular changes. We will continue to evaluate whether SWAP is an important addition to the ophthalmologist's armamentarium for diagnosing glaucoma.

Retinal Topography

The GDx machine uses a laser disc confocal scanning ophthalmoscope to obtain topographic images of the optic disc and periparillary retina. An alternative technology Heidelberg retinal topography. The GDx machine can objectively assess nerve fiber layer architecture, particularly the shape of the optic nerve.

The current problem in using these technologies is that even with slight movement of the eye, the machine's printout can record a rating of both abnormal nerve fiber layer and normal nerve fiber layer within 1 week when absolutely no change has occurred. We now use Heidelberg retinal topography as another adjunctive source of information, but at the present time do not find it any more valuable for making decisions than excellent stereo photographs. Each generation of lasers, however, is showing improvement. The work that Wayne Abb/Rob Weinreb, at the University of California, San Diego and his group have done in San Diego should yield results that will be more reproducible. At present one should not treat a patient based only on results with the GDx machine or Heidelberg. Instead, treatment is based on the examination of the optic disc, stereophotographs, and the overall clinical picture.

Frequency of Examination

How frequently to evaluate a patient depends upon a number of factors. Taking a thorough family history and determining the patient's general physical health are important steps toward making this decision. If patients have retinal vascular disease, diabetes, or a strong family history of glaucoma, we evaluate them more often. We are also more cautious when patients are under treatment for other entities, whether high cholesterol or a disease requiring other systemic medications. The overall vascular status of the patient is an important consideration for the ophthalmologist in deciding if and when to lower the intraocular pressure in order to

prevent visual field loss. If a patient has one or two family members with a strong history of glaucoma but is himself relatively healthy, eats well, and exercises, we recommend a yearly evaluation. If the patient has healthy looking tissue, 0.2 to 0.5, yearly evaluation is appropriate. Yearly evaluation is also appropriate for patients with a smaller cup-to-disc ratio. Patients with 0.6 to 0.7 and a family history of glaucoma should be evaluated every 6 months. (Some authorities advise more frequent evaluations – Editor). It is important to establish parameters for evaluating progression and for deciding on treatment. Although intraocular pressure is not the only concern, it is an important one, particularly when it increases significantly. Whereas if a patient´s pressure rises from 18 or 19 to 22 after 1 year, this is not a cause for too much concern but it would be if the pressure rose to 25 after just 1 year. Pressure is still a significant risk for damage to the optic nerve, regardless of the other parameters.

Chapter 3
EVALUATION OF THE OPTIC DISC IN THE MANAGEMENT OF GLAUCOMA

George Spaeth, M.D.

Optic disc evaluation is at the heart of the evaluation of the patient with glaucoma. Disc examination is not completely objective because it requires some interpretation by the ophthalmologist. However, it is far more objective and reproducible than is examination of the visual field. We believe that evaluation of the disc should focus on whether or not the disc appearance has changed. Determination that change has occurred is often impossible to make based on a single observation. Therefore, conclusive evidence that a disc is damaged often requires consecutive disc evaluations. Consider the patient who presents with a disc with moderate cupping (Figure 1). On the basis of one evaluation the ophthalmologist cannot tell whether this disc is healthy or pathologic; it cannot be determined whether the disc is enlarging in a concentric fashion or whether the patient was born with a cup already that size. Such an evaluation demands consecutive examinations.

However, some indications of disc abnormalities are apparent even on one examination. The most characteristic change is the acquired pit of the optic nerve (APON), which is a pathognomonic sign of glaucoma damage (Figure 2). This APON is a localized loss of tissue immediately adjacent to the outer edge of the rim. (The concept that this notch in the disc is an "acquired pit of the optic nerve" is not universally accepted – Editor). It appears shiny and is usually located slightly temporal to the superior or inferior pole. Two thirds of APON's are inferior. Usually some associated peripapillary atrophy is adjacent to that area. The presence of an APON does

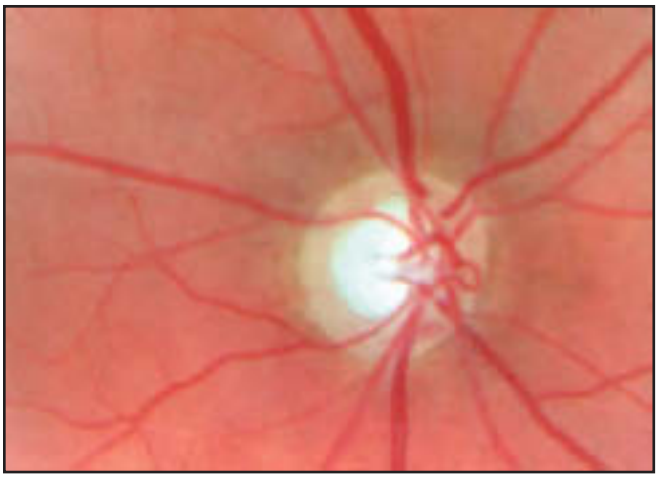


Figure 1: Disc with Moderate Cupping - Conclusive Evidence that a Disc is Damaged Often Requires Consecutive Disc Evaluation

Moderate-sized cup with a moderately thin rim. One cannot tell whether this is congenital or acquired cupping. There are no field defects in this eye. Further evaluation of the patient, including consecutive evaluation of the discs, is necessary.

not necessarily indicate that damage is continuing, but it is a definite sign the patient has been affected by the process of glaucoma. Another finding typical of glaucoma is a disc hemorrhage that crosses the rim (Figure 3). A close association exists between disc hemorrhages and APON's. The hemorrhage may precede the development of the APON. The pathogenesis of these hemorrhages is still speculative.

Other signs that alert the ophthalmologist to the possible presence of glaucoma on just one examination include asymmetry between the two optic

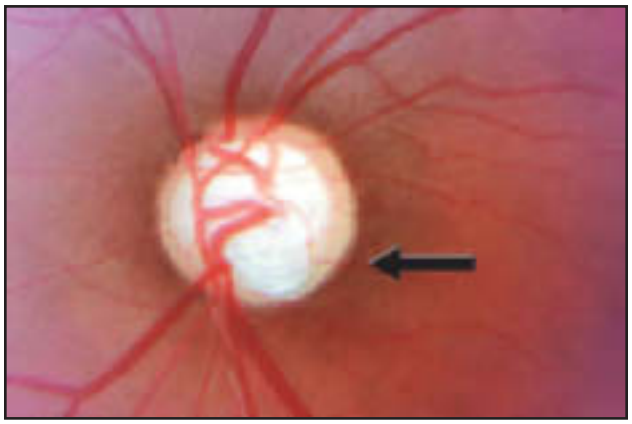


Figure 2: Significance of APON, Pathognomonic Sign of glaucoma Damage

A patient with a notch inferiorly, and an acquired pit of the optic nerve directly at the outer edge of the rim at 5:30 (see black arrow).

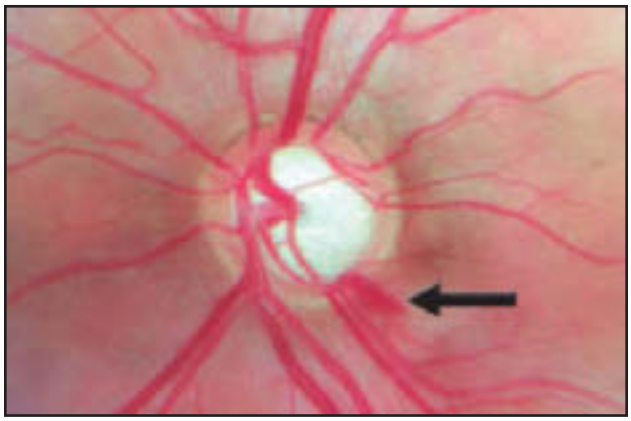


Figure 3: Disc Hemorrhage Crossing the Rim

Characteristic disc hemorrhage crossing the rim of the optic nerve (see black arrow). This type of hemorrhage is most frequently seen in patients with glaucoma in association with low intraocular pressures, and is often a sign that the glaucoma is uncontrolled.

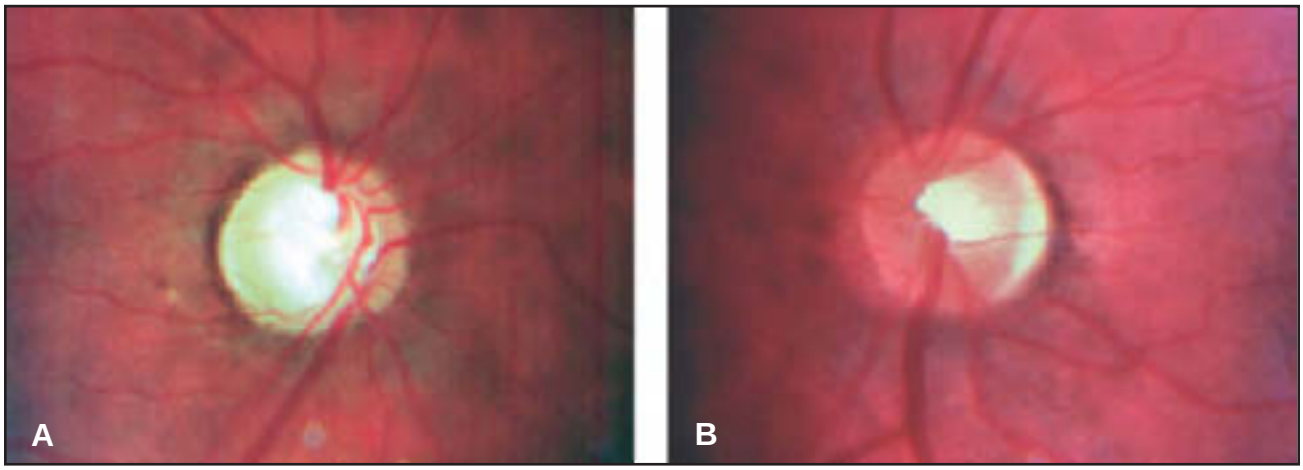


Figure 4 A-B: Significance of Asymmetry Between the Two Optic Nerves

(A-right eye) A very thin rim suggestive of glaucoma, which becomes more convincing when compared with the appearance of the other eye shown in (B-left eye), in which the disc is clearly healthier.

nerves (Figure 4, A,B). A marked focal change and a notch in the rim inferiorly in only one eye but not the other is highly suspect (Figure 5). Even a notch by itself is a sign of great concern; a unilateral notch is almost never associated with a normal eye (Figure 6). Asymmetry alone is also suggestive of possible glaucoma, but other potential causes for asymmetry, such as a difference in the size of the discs, typical of anisometropia or congenital defects, must be ruled out. This requires estimating the size of the disc (Figure 7).

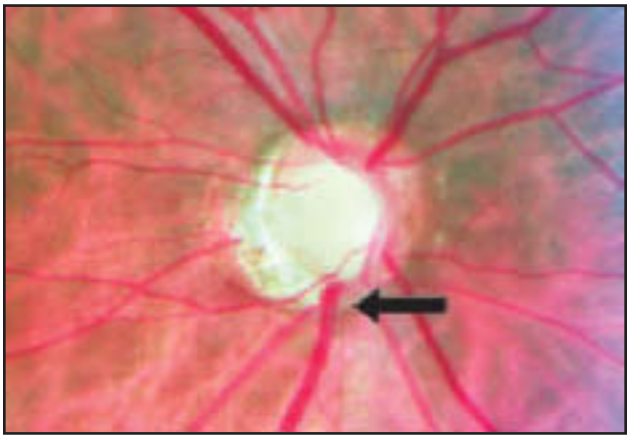


Figure 5: Bayonetting Vessel Adjacent to Pathologic Notch, Highly Suspicious of Glaucoma

An atypical disc with peripapillary atrophy. However, careful consideration of the disc in Figure 5 at the 6 o,clock position shows a sharply bending or bayonetting vessel adjacent to a pathologic notch (shown by arrow). If the fellow eye does not have a similar picture, this is highly suspicious of glaucoma.

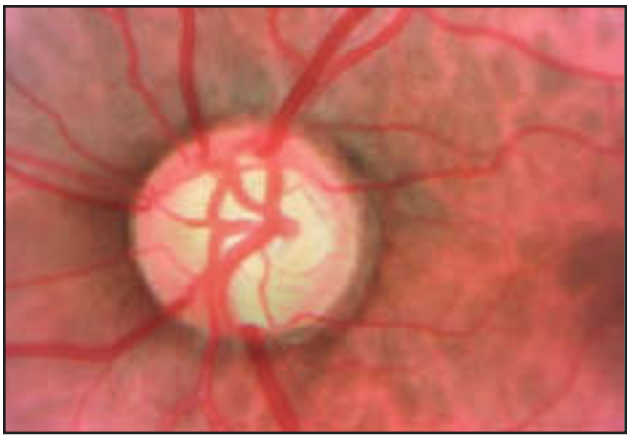


Figure 6: Unilateral Notch Characteristic of Glaucoma

In this patient, the disc is sufficiently characteristic, due to the localized notch at the 6 o,clock position that a diagnosis of glaucoma is almost certain.

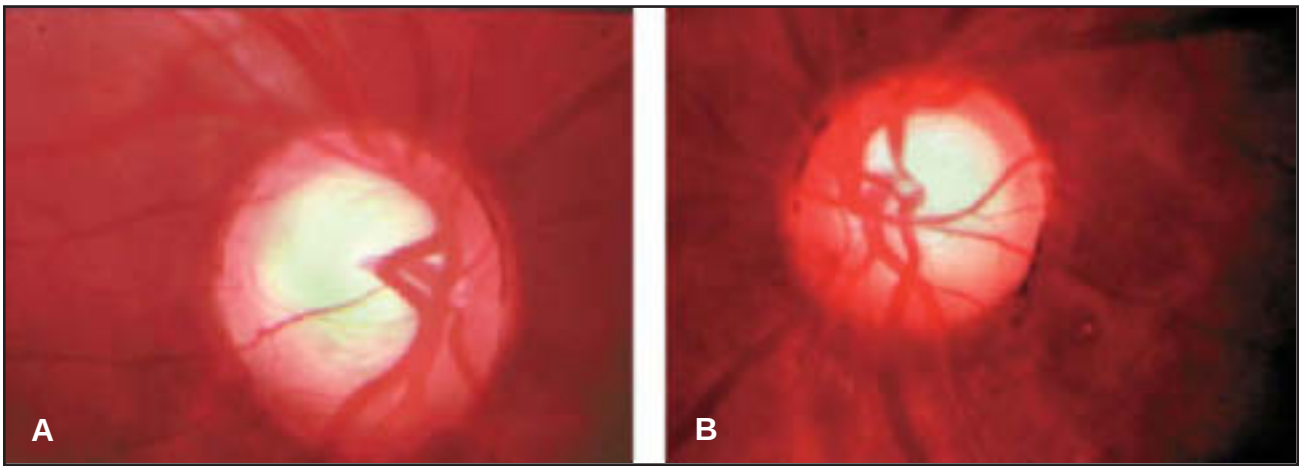


Figure 7 A&B: Asymmetry Alone is Suggestive but Not Pathognomonic of Glaucoma - Importance of Estimating Size of Disc

These photographs were taken at the same magnification, yet note that the optic nerve in the right eye (A) appears considerably larger than that in the left (B) . The cup in the right eye may appear larger, but in actuality, the right optic nerve is the healthier of the two, because the rim is actually a bit thicker comparatively in the right eye than in the left.

Conducting the Optic Disc Evaluation

We prefer to look at the disc itself, using a technique that can be used around the world. We use a direct ophthalmoscope to provide good magnification, and a 60 diopter (D) or 90D lens to provide stereopsis at the slit lamp. The direct ophthalmoscope is used very carefully to allow for the best possible visualization. Even with meticulous direct ophthalmoscopy, it is sometimes difficult to obtain a sense of stereopsis and depth of the cup. As Gloster and Primrose pointed out many years ago, a large beam that encompasses more than just the optic nerve causes the color of the retina to bleed into the optic nerve itself, making it much harder to detect and localize areas of pallor. Moreover, the depth of the cup cannot be determined with a large beam because of the absence of shadows. It is the presence of shadows that makes it possible to turn a two-dimensional image into the three-dimensional image necessary for evaluation.

A Hruby lens or a contact lens can provide excellent visualization, but these lenses may be somewhat difficult to use. The contact lens usually requires the use of a bonding solution, such as methylcellulose which blurs the patient's vision, thereby interfering with later refractive, visual field or photographic examination. Therefore, I prefer to use a technique that does not require a bonding solution.

Recording the Disc Image through Drawing

How should the image be recorded when the optic disc is visualized? To use a disc drawing is preferable. This is not because we think we can draw as accurately as a photograph records an image. But we can see things the photograph cannot record. More important is the learning experience and discipline that come from examining the disc thoroughly enough to make a careful drawing. When looking at a disc and drawing it carefully, the ophthalmologist maintains his observational skills.

The importance of practice to maintain skills is well illustrated through an example from the life of the pianist Arthur Rubenstein. Even after he was acclaimed as one of the world's greatest pianists, Rubenstein continued to take piano lessons. Rubenstein said that when he didn't practice for 1 day, he could hear the difference in his playing. When he didn't practice for 2 days, his wife could hear the difference, and when he didn't practice for 3 days, the audience could hear the difference. In a similar way we believe that examining and drawing the disc becomes a constant training experience.

First, outline the shape of the disc. Discs are usually not round but oval or irregular. A template that outlines a round disc with space to sketch the cup inside guarantees that the disc will be drawn improperly. The ophthalmologist must outline the shape of the disc himself or herself . Then, within the shape, the rim is defined. The direct ophthalmoscope monocularly visualizes changes in the configuration of the blood vessels, which are most helpful. Color is also helpful, but it can be misleading. To define the rim clearly, a 60D or 90D lens aids in better estimation through the stereopsis it affords. During the drawing process it is useful to return frequently to the direct ophthalmoscope. Special attention is paid to the superior and inferior temporal areas to ensure there is no acquired pit or disc hemorrhage. The rim in those areas should be drawn especially carefully. Note whether the blood vessels are bayoneted and whether peripapillary atrophy is present. Then the amount of pallor, from 1+ to 4+, should be assessed and commented on. Figure 8 illustrates the drawings of discs shown in Figures 1, 2, and 5.

Only when the drawing is complete, we look at our previous drawing or disc photograph. This can be a humbling experience. Sometimes we find we have missed something or have drawn something we missed before. But we also find that the more practice we have in identifying relevant features, the better his drawing skills become.

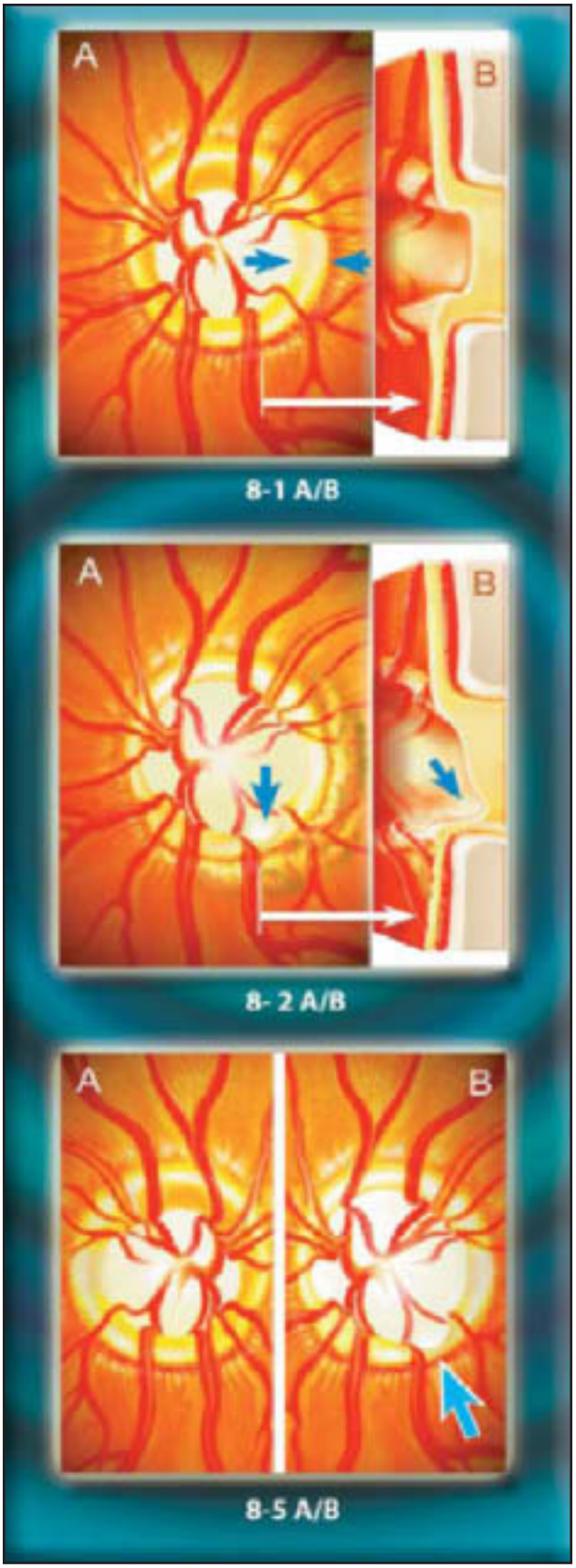


Figure 8-1 AB: Determination of Change in the Optic Disc

Figure 8-1 AB is a drawing of the optic disc in the same patient shown in Fig. 1. The latter, however, is a color photograph of the same optic disc. Whether using color photographs or drawings, an evaluation of the optic disc should include consecutive evaluations overtime to observe if any change is taking place. In a disc, such as the one shown with moderate cupping (A), a single evaluation cannot determine if glaucoma is present or if the patient was born with a cup that size. Moderate cupping is noted by the size of the rim (area between blue arrows). (B) shows the same disc in cross section.

Figure 8-2 AB: Disc Abnormalities More Determinate of Glaucoma

Figure 8-2 AB is a drawing of the optic disc in the same patient shown in Fig. 2. The latter, however, is a color photograph of the same optic disc. Figure 8-2 "A" shows one most characteristic change in the optic disc that can signify the presence or past occurrence of glaucoma. This refers to the acquired pit of the optic nerve (blue arrow). This is a localized loss of tissue immediately adjacent to the outer edge of the rim. It appears shiny and is usually located slightly temporal to the superior or inferior pole. The corresponding cross section (B) shows the extent of the tissue loss in this area.

Figure 8-5 AB: Presence of Glaucoma Noted by Asymmetry Between Two Optic Nerves

Figure 8-5 AB is a drawing of the optic disc in the same patient shown in Fig. 5. Figure 8-5 AB show another sign that can alert to the presence of glaucoma in just one examination. This refers to asymmetry between the two optic nerves. A marked focal change and a notch in the rim inferiorly in only one eye but not the other is highly suspect. Note that eye (A) shows moderate cupping with no visible notch. Eye (B) of the same patient shows increase cupping and a notch (arrow) in the rim. A unilateral notch is almost never associated with a normal eye.

Reproducing the Disc Image through Photography

Another method for evaluating the optic disc is photography. A photograph provides a hardness (which may obscure details – Editor) not present in disc drawings. The danger of relying on a two dimensional photograph is that without stereopsis it is very difficult to visualize the shape of the cup. Moreover, the flash illuminates the entire retina and bleeds into the disc, minimizing the ophthalmologist's ability to detect pallor. Stereoscopic photographs offer an improvement. Changing the position of the camera provides a sense of stereopsis but it does not allow comparison with a previously taken set of photographs because the base shift will not be the same. For instance, a stereoscopic bowl that is actually unchanged may appear deeper simply because the base of the stereoptic shift was changed.

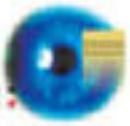
Consequently, the best photographic technique uses a fixed distance between images. A good example is the Canon fundus camera, which provides simultaneous stereoscopic photographs printed out on the same slide. The disadvantage of this technique is the lack of capacity for magnification. Because the photograph is smaller to begin with, the ophthalmologist needs a viewer that provides enough magnification to visualize the important details.

Image Analysis of the Optic Disc

Image analysis, offers hope for improving optic disc evaluation in the future. Some techniques are already fairly reproducible. Heidelberg Retinal Tomography device (HRT), evaluates the topography of the disc using confocal laser scanning and taking the surface of the retinal nerve fiber layer as an arbitrary reference plane. It defines the nature of the disc in a particular plane and then progresses posteriorly through the disc, making cuts in additional planes. On the basis of those cuts it reconstructs the structure of the optic disc in three dimensions. Measurements from the HRT are quite reproducible. It has the advantage of being digitized so the results can be quantitative. This means that in repeating the machine's analysis, one has a specific measure of the degree of damage. For example, the HRT can show that the cup has deepened, say, 25 microns in a particular area, providing a good sense of the amount of change that has occurred. The problem is that in comparing one image with the next, the validity of change depends strongly upon the ability to register those two images exactly. If there is a saccade that has moved the eye so the gaze is a little to one side, the image registered the second time will not be identical to the image registered the first time. The difference in image can be corrected to some extent but not completely, by software programs.

Determination of Retinal Nerve Fiber Layer Thickness

Another method, optical coherence tomography (OCT), measures the actual thickness of the retina by using a raster technique. This method actually measures the thickness of the nerve fiber layer. It is a difficult technique, and software to support the analysis has not yet been fully developed. Although there are some optical problems to be worked out, this method may prove very beneficial in the future. (**Editor's Note**: This is an important, new concept. Detection of retinal ganglion cell derangement may permit the earliest objective determination of glaucoma damage, before functional change in visual field or the gross loss of disc (cup) structure can be appreciated.)



Another technique, called a nerve fiber layer thickness analyzer or polarimetric technique, does not directly measure thickness. When light passes through the ganglion cell layer, it becomes polarized. The amount of polarization of the light is used to estimate the nerve fiber layer thickness. Measuring the amount of retardation of the light as it goes through the layer gives an indirect measure of nerve fiber layer thickness.

Current Limitations of Clinical Usefulness

From a clinical point of view, image analysis techniques have not been demonstrated to be sufficiently valid that patients can be managed based on this data alone. As software and hardware improve, we believe that someday it will be possible to take an image of an optic disc and retake that image 2 years later, or even 6 months later, and determine with real confidence whether or not the condition is deteriorating, remaining stable, or improving. This will be an enormous step ahead because patients with glaucoma are managed primarily on the basis of detecting change.

Using images to diagnose the existence of glaucoma is more complex because patterns must be considered. Whereas an art critic can instantly distinguish between a Monet and a Manet painting, computers could not make the distinction easily. They are not yet programmed to do well with complex pattern recognition.

In summary, we believe that optic disc analyzers and optic nerve image analysis machines are not useful at the present time in deciding whether or not glaucoma is present. If a patient has no nerve fiber layer left, the nerve fiber layer analyzer can obviously tell that the nerve fiber layer is gone. (**Editor's Note:** The ophthalmologist can also tell this by using red-free light from the ophthalmoscope). Long before that stage, however, this diagnosis could easily have been made simply with an ophthalmoscope. From the diagnostic point of view, these analyzers are neither sufficiently sensitive nor specific. However, they may be helpful for detecting change. We believe they will become even more useful in the not-too-distant future.

The Cup/Disc Ratio

Even a century ago, atlases like the masterwork published by Fornieger contained drawings similar to those published in HIGHLIGHTS. The key difference, however, is that those early drawings were generated by what could be called an analog technique; they were not quantitative in any way. With the introduction of more scientific methods into the study of medicine and into clinical practice came the introduction of measurement. An enormous step forward was made by the introduction of the concept of the cup/disc ratio primarily by Armaly, who said that the size of the cup in comparison to the entire disc was the key principle. Then it became apparent that certain cup sizes were inherited. For instance, in black patients the cup/disc ratio tends to be larger than in white patients. New awareness about measuring cup size led to studies determining how the cup changes.

At present we do not teach our residents to use cup/disc ratios. As a matter of fact, we even discourage use of the term. This is because so much gets lost in the measurement. First, the cup/disc ratio is difficult to determine. Studies by **Paul Lichter** and others have shown that clinicians are not particularly

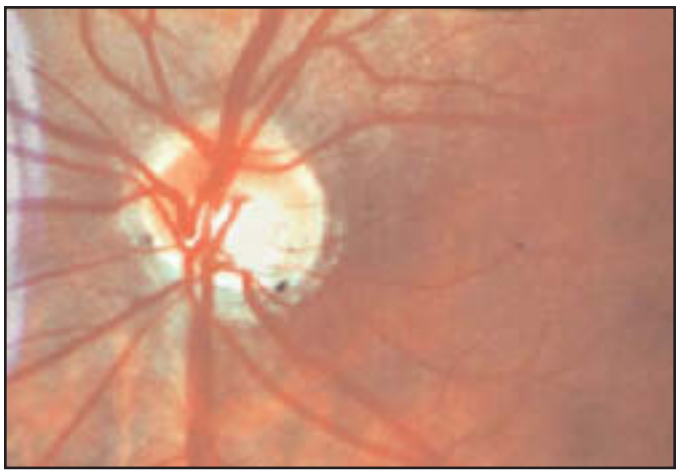


Figure 9: Controversies of Cup - Disc Ratio

This optic nerve head shows a small cup/disc ratio. However, the disc is highly pathologic, with a notch which is characteristic of damage occurring in glaucoma. The cup/disc ratio in this case could be misleading, whereas an evaluation of the rim-disc ratio would be highly revealing.

good at measuring cup/disc ratio in a reproducible way. This problem is less severe when comparing two readings by the same ophthalmologists rather than two readings by two different ophthalmologists. In other words, intra-observer reproducibility is more reliable than inter-observer reproducibility. Figure 1 shows a disc with a large cup/disc ratio. However, there would be no field defect in this eye. In contrast, figure 9 shows a disc with a smaller cup/disc ratio, but this is a sick disc, and would be associated with a marked loss of visual field.

But the cup/disc ratio captures only a particular aspect of the disc. Recent image analysis machines do a much better job of assessing the overall profile of the disc. They measure the width of the rim not just in horizontal or vertical terms but in many dimensions. For instance, they may conclude that the rim is becoming narrow between the 5 o'clock and 6' o'clock positions. This change, which might not show up on a cup/disc ratio analysis at all, may be a very valid sign of the worsening of glaucoma. And, of course, the cup/disc ratio also omits important signs such as pits, notches, hemorrhages, and signs of disc damage that are related to changing patterns.

Chapter 4
ADVANCES IN VISUAL FIELD TESTING

Joel S. Schuman, M.D.
Zinaria Y. Williams, M.D.

Developments in visual field testing have aimed at newer strategies for earlier detection of visual damage in glaucoma. Early automated testing strategies were time-consuming; and at times, tests lasted more than 20 minutes per eye. Such long examinations sometimes resulted in patient fatigue and reduced patient compliance. The most commonly used older algorithm is the standard full threshold program.

Clinical Applications of New Family of Tests

Swedish interactive threshold algorithms (SITA) (Humphrey Systems, Dublin, California) are a new family of test algorithms developed to reduce significantly the test time of thresholding algorithms without a reduction in data quality. Clinical trials in healthy and glaucoma patients have shown that the SITA strategies are fast and accomplish the same or better test quality as do the full threshold program.

Recently, short-wavelength automated perimetry (SWAP) (Humphrey Systems, Dublin, California) has shown potential for earlier detection of glaucomatous visual field defects and more sensitive assessment of visual field progression. The test uses a bright yellow background with blue stimuli. SWAP requires detection by the short-wavelength cones and processing through the small bistratified ganglion cell (blue-yellow). One obstacle to the interpretation of SWAP fields is the presence of greater long-term variability in normal subjects, which makes differentiation between random variations and true progression more difficult.

(**Editor's Note: Richard Parrish, M.D.**, Professor of Ophthalmology at the University of Miami and the Bascom Palmer Eye Institute emphasizes that the **SITA-standard 24-2** has dramatically reduced the amount of time involved in initial visual field testing, and has become the conventional initial visual field test used at the Bascom Palmer Eye Institute. It has essentially replaced the full threshold 24-2 test. Patients are very appreciative of the shorter time involved in the SITA-standard test.

Parrish recommends testing with the 10-2 program if the visual field is limited to a central island to save a great deal of time and patient frustration. The initial criticism that automated fields took too long from the patient's standpoint was absolutely valid. The time saved also contributes to more accuracy as fatigue as a factor is reduced or eliminated.)

Frequency doubling technology (FDT) perimetry (Welch Allyn, Skaneateles, New York, and Humphrey Systems, Dublin, California) provides a useful complement to conventional automated perimetry test procedures and can serve as an effective initial visual field evaluation for detection of glaucomatous visual field loss. FDT isolates a subgroup of retinal ganglion cell mechanisms in the magnocellular (M-cell) pathway. These ganglion cells have functions that are recognized to be abnormal in glaucoma. Because of its high sensitivity and specificity in detecting glaucomatous visual field defects, FDT is currently being evaluated for its potential in screening for glaucoma.

Role of Multifocal Electroretinogram (ERG)

Other developments targeting early detection of visual damage include electrophysiologic testing. This technique may permit objective, quantitative measurement of ganglion cell and optic nerve function, and may be particularly useful in glaucoma. Since the standard electroretinogram (ERG) records a non-specific mass response of the retina, the details of localized change in different regions of the retina are difficult to observe. The multifocal electroretinogram (mERG) has the ability to examine local retinal responses. E. Sutter and D. Tran detailed a method for recording the mERG which allows many retinal areas to be independently stimulated according to a binary m-sequence. The mERG is not dependent upon a subjective patient response and therefore may be more sensitive than standard automated perimetry in detecting early damage to the ganglion cell layer.

Multifocal electroretinography stimulates 103 areas of the central 50 degrees of the retina simultaneously. Patient response is not necessary; a contact lens electrode automatically detects retinal sensitivity. The electrophysiologic responses are organized geographically to produce a functional map of the retina, similar to visual field testing. Multifocal electroretinography is a promising technology for glaucoma detection and progression. Figure 1 is a digital color illustration showing a nor-

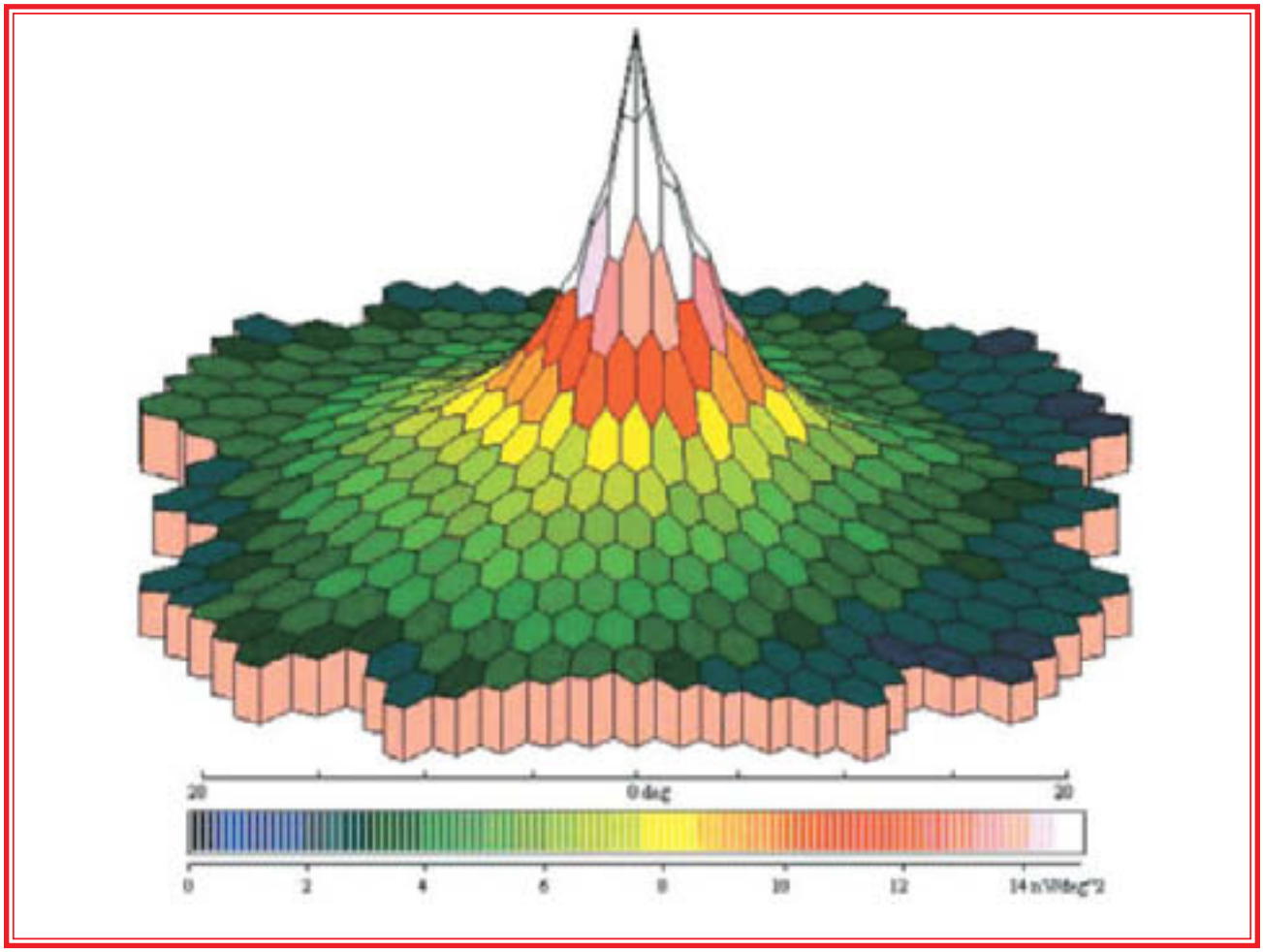


Figure 1: Digital color illustration showing a normal mERG. Note the gradual incline from the periphery to the high central peak, demonstrating maximal light sensitivity.

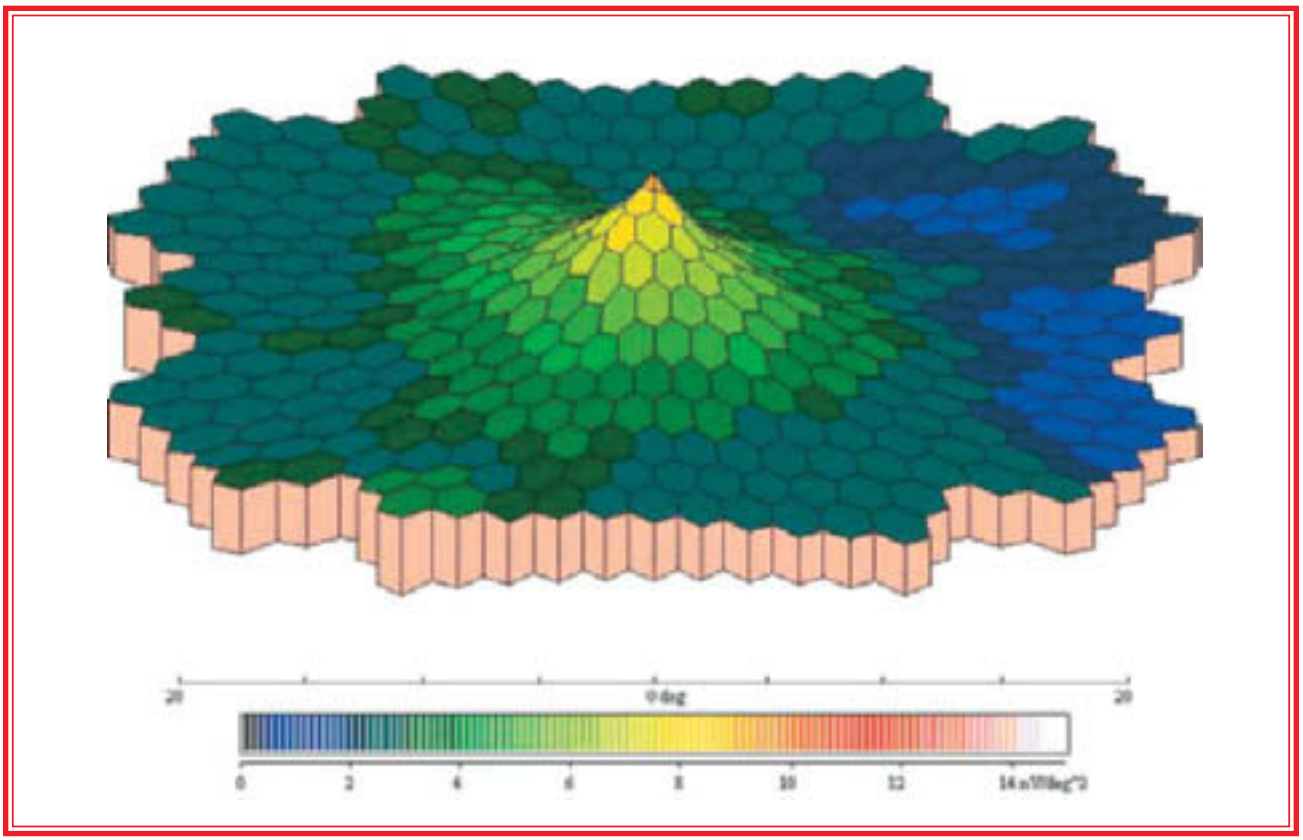


Figure 2: mERG of an eye with advanced glaucoma. There is generalized depression, with a superior arcuate scotoma. The geographic map forms a valley (depression) superior to the peak that corresponds to a superior arcuate scotoma.

mal mERG. Note the gradual incline from the periphery to the high central peak, demonstrating maximal light sensitivity. Figure 2 displays an eye with advanced glaucoma. There is generalized depression, with a superior arcuate scotoma. The geographic map forms a valley (depression) superior to the peak that corresponds to a superior arcuate scotoma.

Significance of Visually Evoked Response (VER or VEP)

The visually evoked cortical potential (VECP, but also abbreviated VEP or VER for visually evoked response) is an electrical signal generated by the occipital visual cortex in response to stimulation of the retina by either light flashes or by patterned stimuli. Pattern VEPs are now preferred over flash VEPs for the evaluation of the visual pathways, owing to their enhanced sensitivity in detecting axonal conduction defects. The response is usually evoked with a checkerboard pattern in which the black and white checks alternate at a frequency of 2 to 10 times per second (2 to 10 Hz). The VEP is primarily used to identify visual loss secondary to diseases of the optic nerve and anterior visual pathways. Recent studies by S. Graham and coauthors have shown correlations between the VEP and visual field defects, but much more work remains to be done in this area prior to clinical adoption of this technique.

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Chapter 5
OPTICAL COHERENCE TOMOGRAPHY (OCT) and RETINAL TOMOGRAPHY

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OPTICAL COHERENCE TOMOGRAPHY (OCT)

Objective Test for Evaluation of the Nerve Fiber Layer

Optical coherence tomography (OCT) is a new and promising technology that allows precise cross-sectional imaging of the eye. It enables non-contact and non-invasive imaging of the nerve fiber layer (NFL) and retina. In the diagnosis, evaluation, and management of glaucoma, OCT is a means of imaging and quantifying nerve fiber layer thickness.

What is OCT?

OCT, manufactured by Humphrey Instruments (Dublin, CA), is a noninvasive, non-contact device that permits high resolution cross-sectional imaging of the retina using light. Similar to computed tomographic (CT) scanning, which uses X-rays, magnetic resonance (MR) imaging which uses electron spin resonance, and ultrasound B-mode imaging which uses sound waves, OCT uses light to perform optical ranging and imaging and thereby achieves the highest resolution of any in vivo imaging technology. OCT has a longitudinal/axial resolution in the eye of approximately 10 microns, with a transverse resolution of the incident beam spot diameter of 20 microns. The measurements of the NFL thickness are obtained automatically by means of a computer algorithm that searches for characteristic changes in reflectivity observed at the superficial and deep retinal boundaries. In approximately 1 second a real-time image is displayed on a computer monitor in false colors, showing a tissue microstructure that appears strikingly similar to a histologic section (Fig. 1-C).

Since OCT is based on near-infrared interferometry, it is not affected by axial length, refraction, or by the degree of nuclear sclerosis; however dense posterior subcapsular or cortical cataracts may impair the ability to perform OCT. OCT requires a pupil diameter of at least 3 mm, which requires dilation in some patients.

Why Is The Nerve Fiber Layer Important?

Nerve fiber layer thinning has been shown to be the most sensitive indicator of glaucomatous damage, preceding both visual field loss and detectable changes in optic nerve appearance. In many cases visual field loss and characteristic changes in the optic nerve head appearance may not be detected even when up to 50 percent of the nerve fibers have been lost.

NFL thickness as measured by OCT demonstrates a high degree of correlation with Humphrey 24-2 visual field defects. Schuman et al have shown that glaucomatous eyes have a significantly thinner measurement of NFL by OCT as compared to normal eyes, particularly in the inferior quadrant. Cupping and the neuroretinal rim area have been shown to correlate with NFL thickness. Interestingly, OCT has also demonstrated thinning of the NFL with increasing age even in healthy eyes.

OCT also offers quantitative and reproducible measurement of macular thickness. R. Zeimer and coauthors have shown that there are large losses in retinal thickness at the posterior pole of patients with glaucoma. His hypothesis that glaucoma can be measured through the assessment of macular thickness has been supported in preliminary OCT studies.

A reduction in NFL thickness of only 10 to 20 microns may be significant, indicating impending visual field loss. Indeed it is ganglion cell death that produces vision loss in glaucoma. Changes in the optic nerve head reflect the atrophy of these cells. The axons of these cells are less compact in the retinal nerve fiber layer than in the optic nerve head and thus easier to evaluate. The utility of OCT in the evaluation of NFL thinning is important in assessing the disease process of glaucoma.

Interpretation of OCT

Nerve fiber layer thickness is measured at a circle diameter of 3.4 mm around the optic nerve. Figure 1-A shows a stereoscopic full color photo-



Figure 1A: Color photograph of a normal optic nerve head.

graph of a normal optic nerve head and Fig. 1-B shows the visual field, which is full.

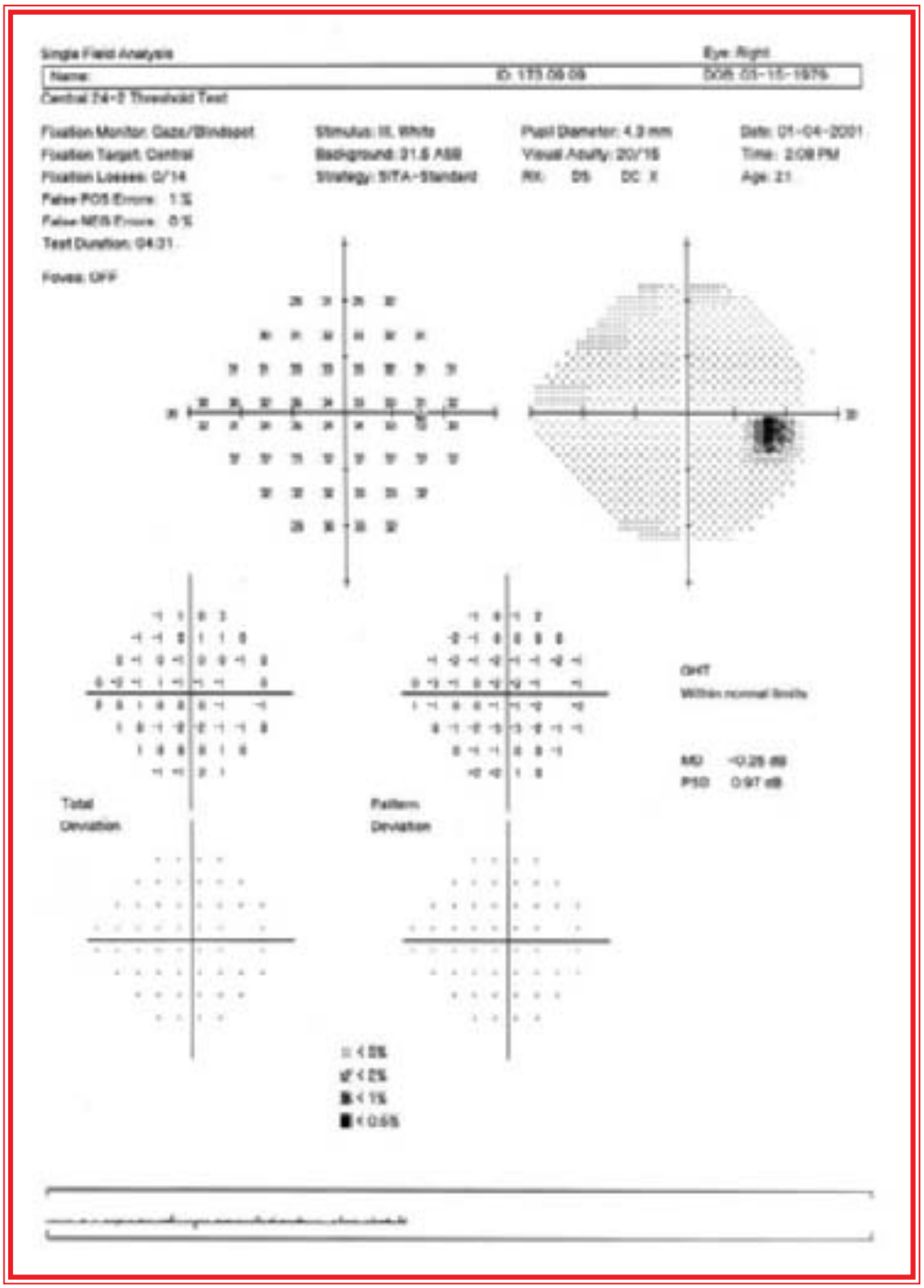


Figure 1B: Full SITA 24-2 visual field of eye shown in Figure 1A.

The OCT is shown in Fig. 1-C. The NFL tomograph is represented by the most superficial red reflectance layer. The numerical NFL measurements of each clock hour and each quadrant are seen on the OCT circular scan in Fig. 1-C. In normal eyes, the NFL is thickest superiorly and inferiorly and thinner temporally, as expected.

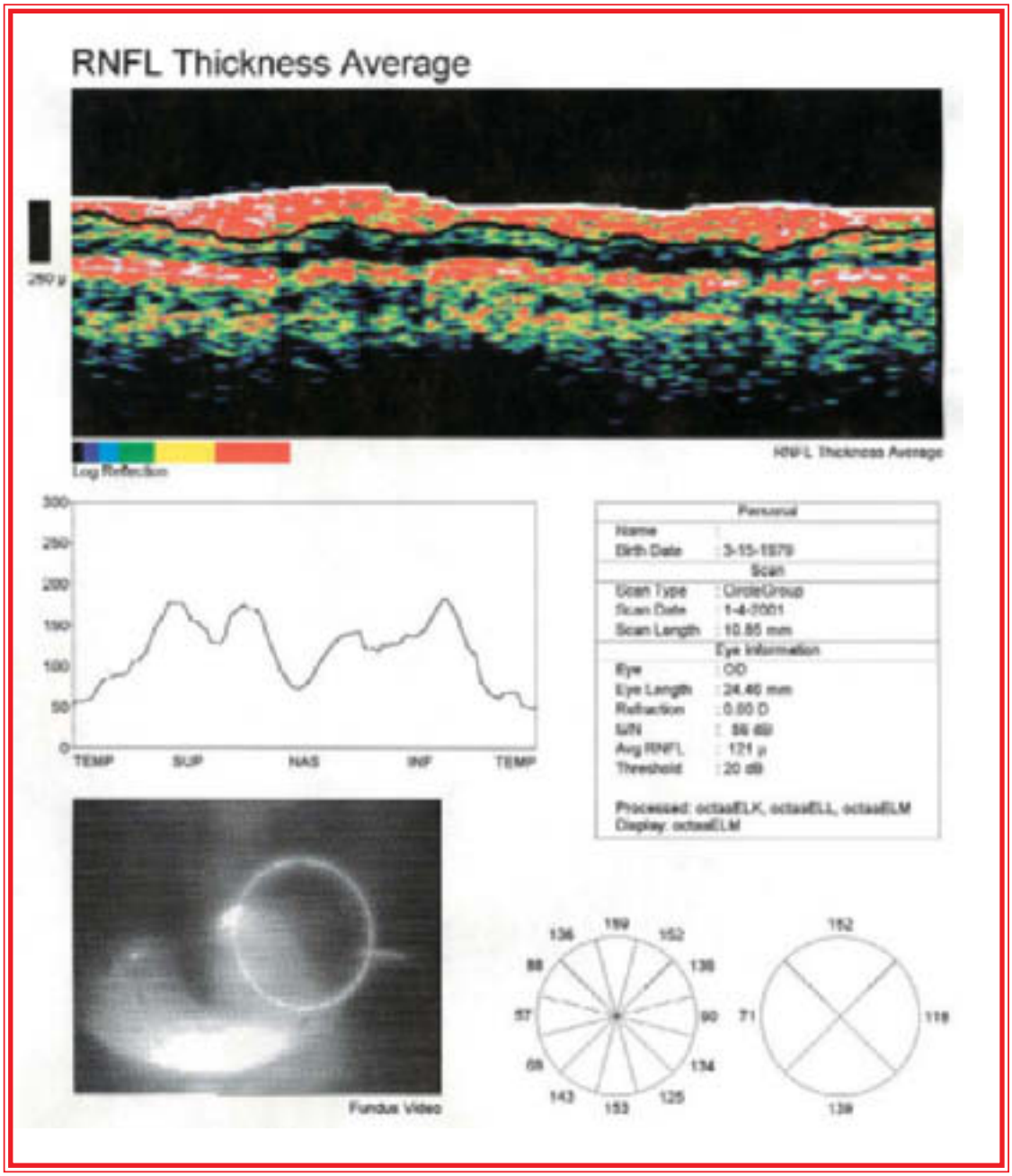


Figure 1C: Optical Coherence Tomography (OCT) of eye shown in Figure 1A. The most anterior red reflectance layer represents the NFL in the OCT. The quantitative NFL measurements overall, and for each quadrant and each clock hour are shown on the OCT circumpapillary scan in Figure 1C. In normal eyes, the NFL is thickest superiorly and inferiorly and thinner temporally, as expected.

In Fig. 1-D an OCT macular scan illustrates normal macular thickness. Areas of thinning in the ring surrounding the fovea can indicate the presence of a pathological process, such as glaucoma.

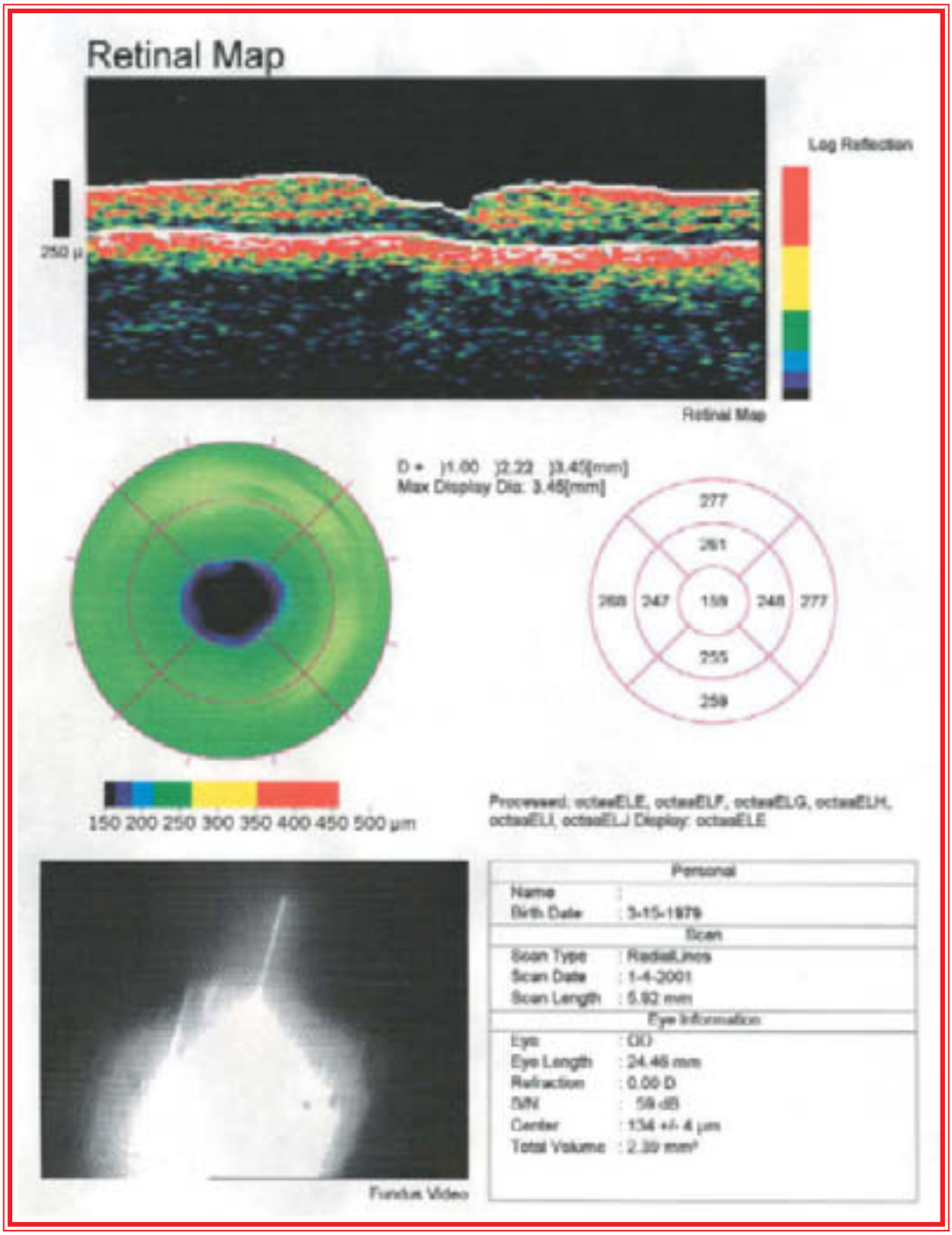


Figure 1D: OCT macular scan of the eye shown in Figure 1A illustrates normal macular thickness. Areas of thinning in the ring surrounding the fovea can indicate the presence of a pathological process, such as glaucoma.

A normative database is currently being created; however, OCT findings to date indicate that the average normal NFL thickness was 105+18 microns using the commercial OCT device.

The optic disc of an eye with early glaucoma is shown in Fig. 2-A.

The visual field shows an inferior arcuate scotoma (Fig. 2-B).

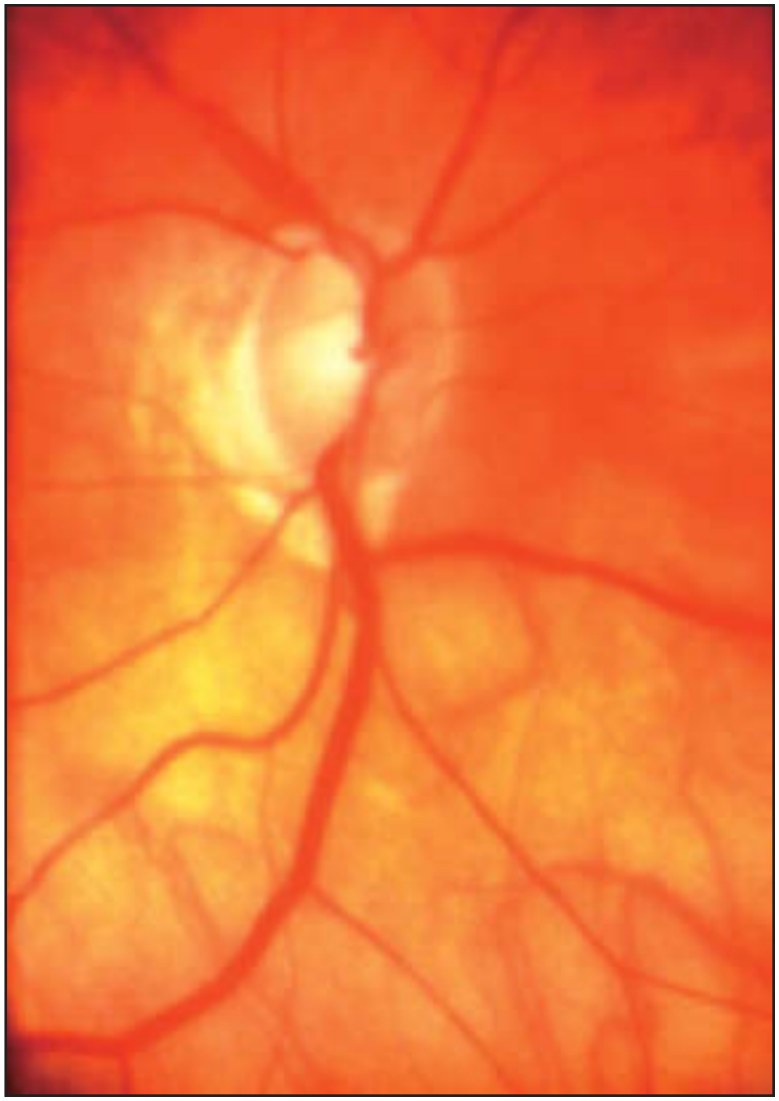


Figure 2A: The optic disc of an eye with early glaucoma

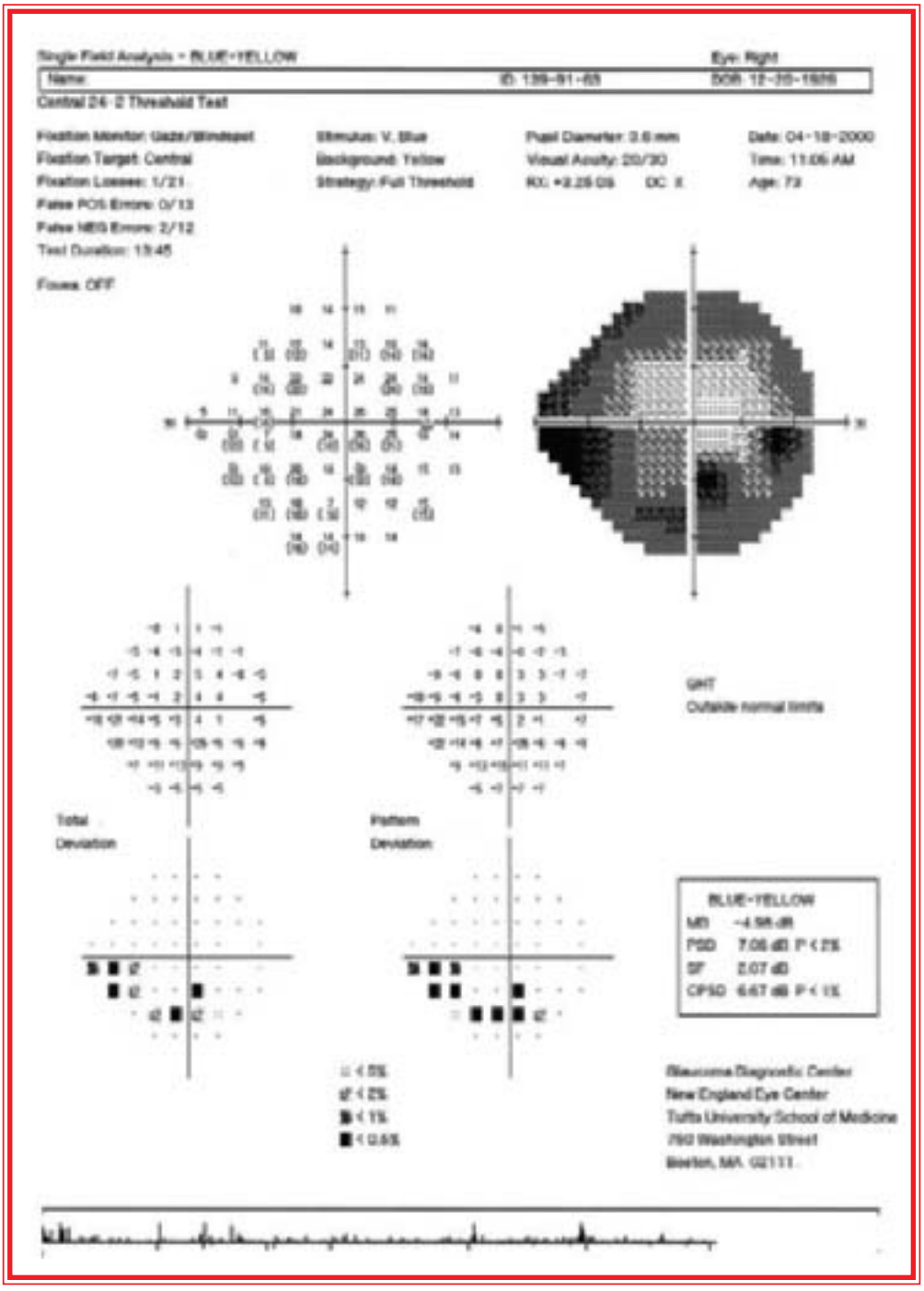


Figure 2B: The SWAP (Short Wavelength Automated Perimetry) 24-2 visual field of the eye illustrated in Figure 2A shows an inferior arcuate scotoma.

The OCT shows localized thinning of the NFL superotemporally as well (Fig. 2-C).

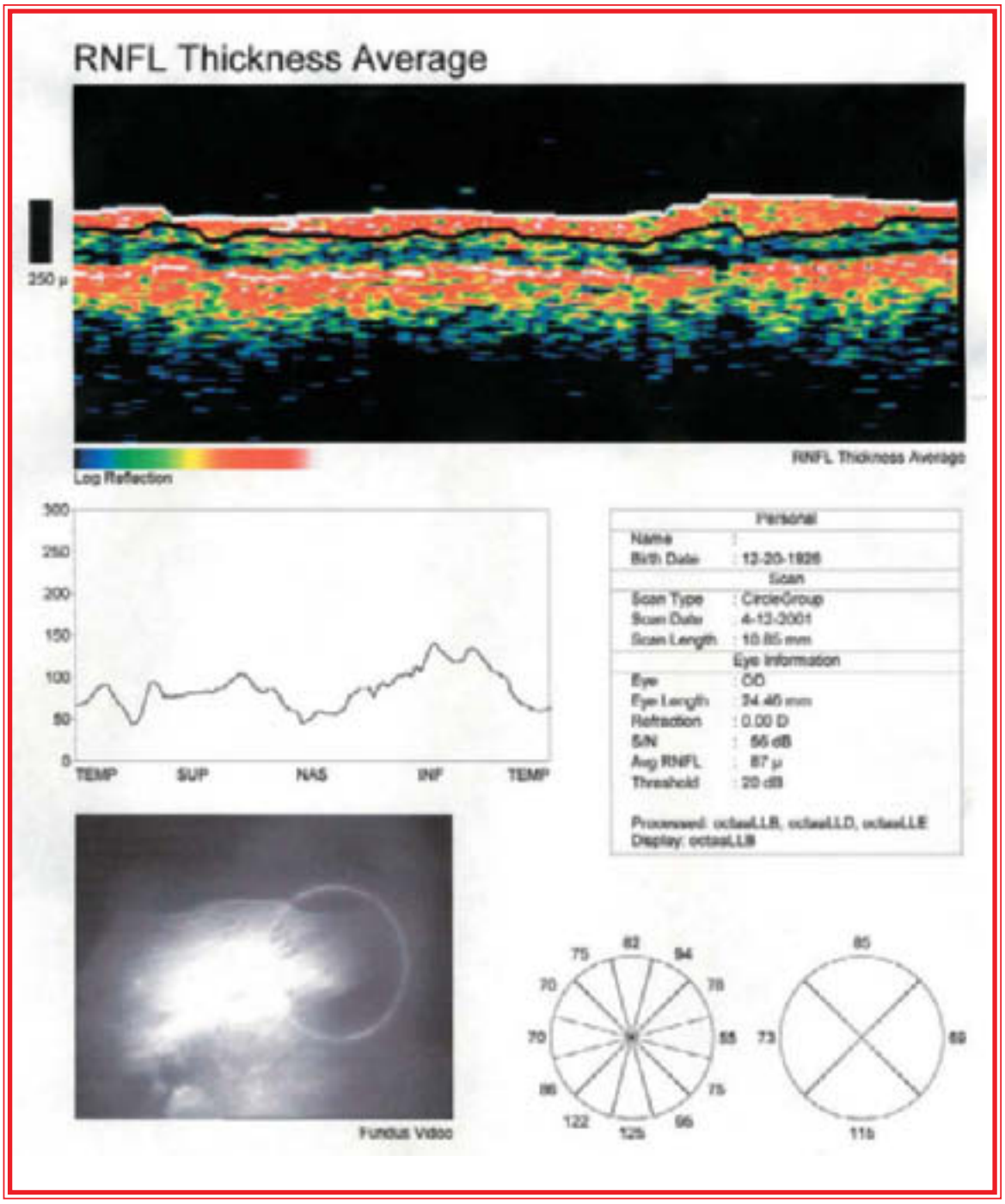


Figure 2C: The OCT of the eye shown in Figure 2A demonstrates localized thinning of the NFL superotemporally, corresponding with the inferior arcuate scotoma.

Advanced glaucoma presents as generalized attenuation of the NFL. The optic nerve photograph in Figure 3-A shows advanced cupping along with severe visual field loss (Fig. 3-B).



Figure 3A: Optic nerve photograph showing advanced cupping, corresponding to visual field abnormality shown in Figure 3B.

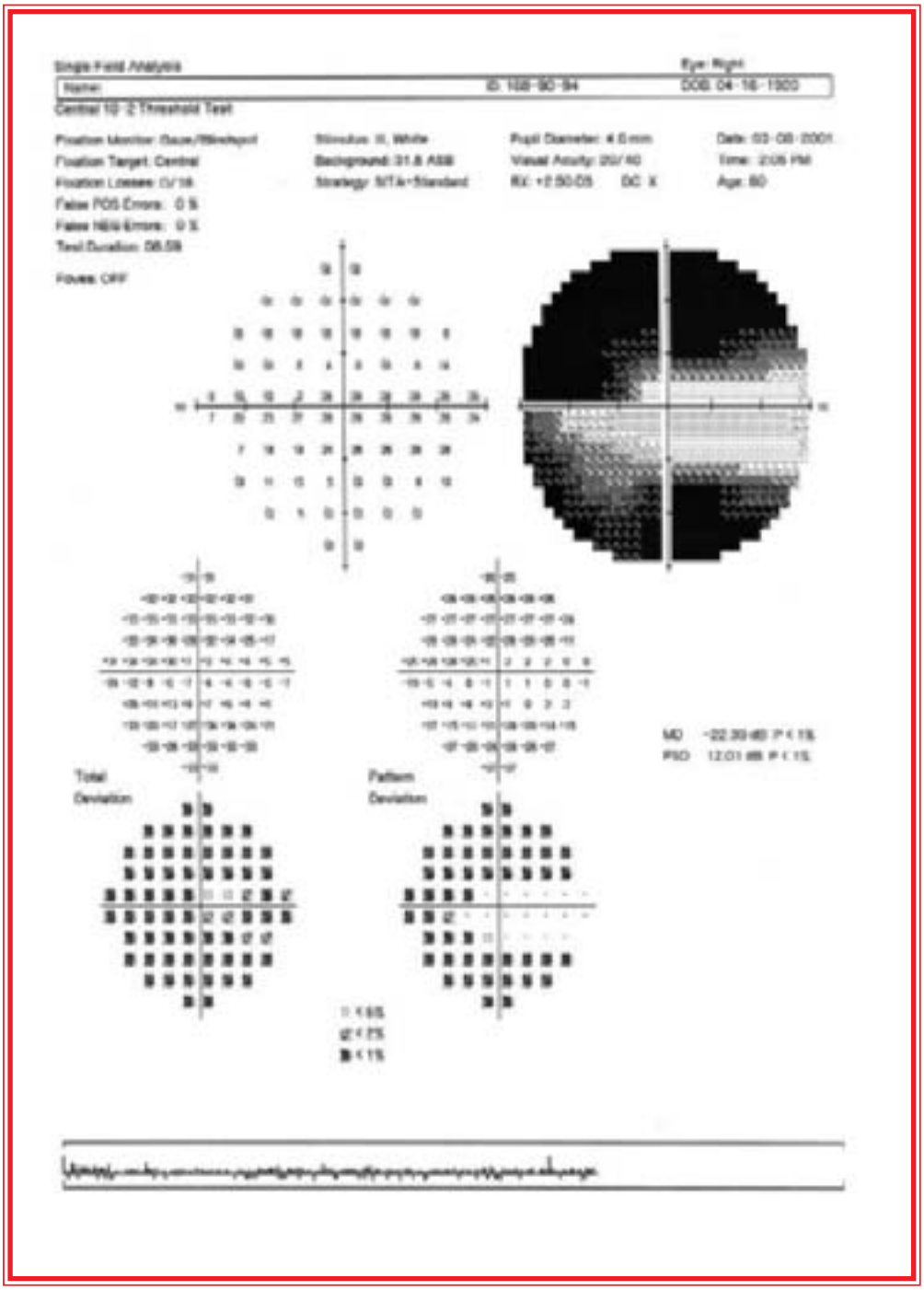


Figure 3B: SITA 10-2 visual field of eye shown in Figure 3A demonstrating corresponding severe visual field loss.

The OCT in Fig. 3-C shows diffuse NFL thinning but more pronounced inferiorly which corresponds with the visual field change.

In essence, optical coherence tomography provides a cross-sectional image and quantitative, objective NFL thickness measurements (Figs. 1-C, 2-D, 3-C). Once a normative database is developed, OCT may help to differentiate between normal and glaucomatous eyes much in the way automated perimetry does but potentially with a much higher sensitivity and specificity. Currently, OCT provides the clinician with objective NFL measurements highlighting focal and more diffuse deficits. OCT may be useful for following individual patients to determine if thinning of the NFL is present, and if it increases with time. It may be a very useful tool in monitoring the progression of glaucoma.

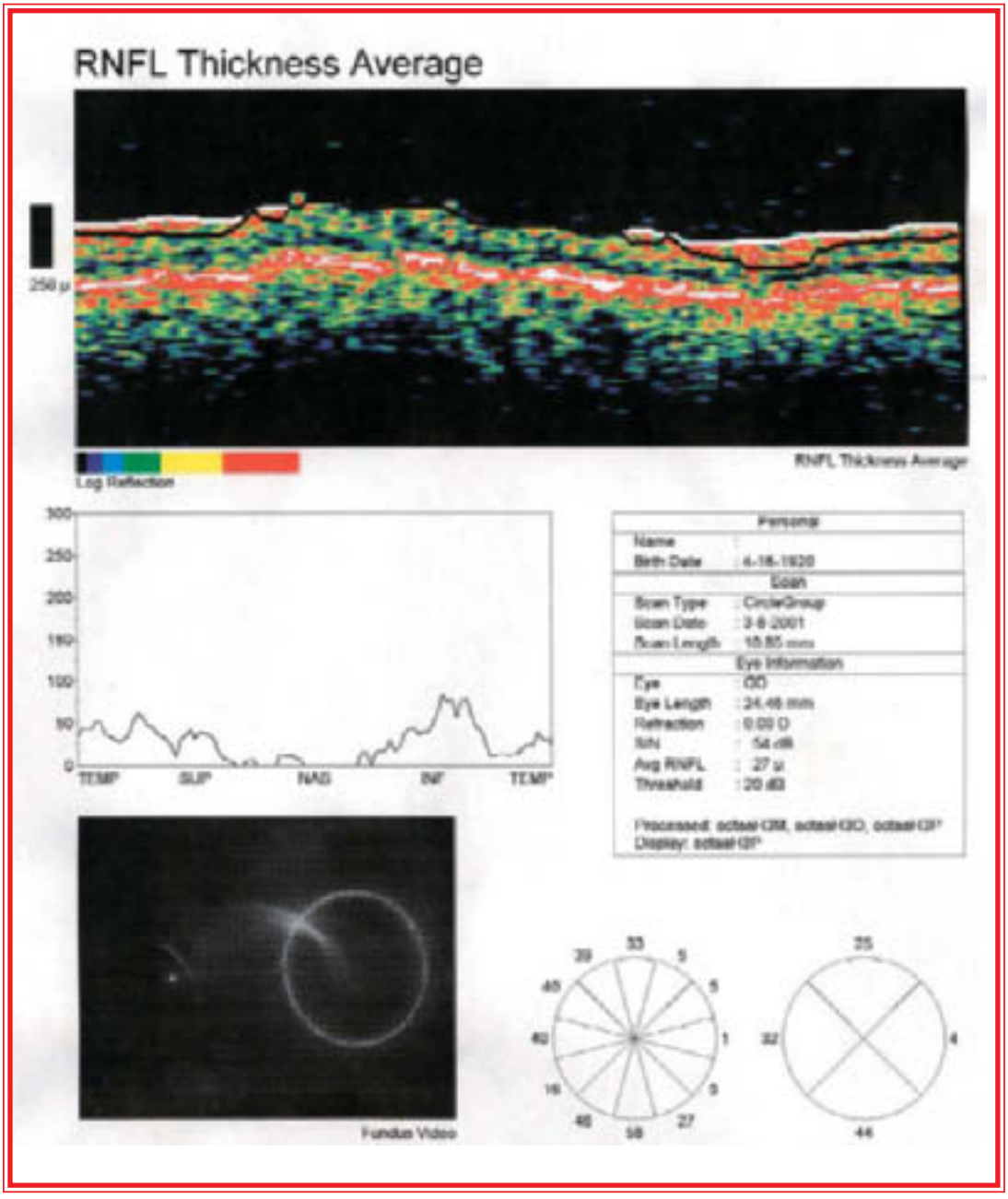


Figure 3C: OCT shows diffuse NFL thinning, more pronounced inferiorly in the area corresponding with the visual field change.

RETINAL TOMOGRAPHY

Retinal tomography is a new technology that produces and analyzes three-dimensional images of the posterior segment and is particularly useful for producing **three-dimensional images of the optic nerve head**. A computerized analysis of this information provides objective estimates of the area of the optic nerve head and cup, the vertical and horizontal cup to disc ratio, the rim area, the ratio of cup to disc area, rim volume, the mean and maximal cup depth, and a three-dimensional image of the cup. The readings for each patient are electronically compared to the data base for normal eyes and the print-out indicates if the readings are within normal limits (Fig. 4A- 4D) or outside normal limits. (Fig. 5A - 5D) The readings are also presented graphically. The instrument is also capable of estimating the mean thickness of the retinal nerve fiber layer along the area exposed to the laser beam, but there is a wide overlap between normal and pathological parameters in nerve fiber layer thickness. For this reason, retinal tomography is not as accurate or useful a measurement of nerve fiber layer thickness compared to the results obtained with ocular coherence tomography.

The retinal tomographer is a confocal ophthalmoscope. In confocal ophthalmoscopy, multiple optical slices are taken of the retina by the laser scanner, (using a Diode laser at 670 nm) and built into a three-dimensional image by the use of appropriate computer software. This image is projected onto a computer screen and can be printed on paper for storage in the patient's chart.

The most important parameters are the horizontal and vertical cup to disc ratio and the cup to disc area ratio. These ratios give an objective measurement of the size of the cup relative to the size of the disc. The data base available for this test carries an overlap between the upper limits of normal and the lower limits of pathology, so that it may be difficult to interpret an individual measurement in an individual patient if the measurement is at the limit of normal. However, in any patient, **repeated retinal tomographies** are extremely valuable in assessing whether there is progression of the size of the cup in relation to the disc margin or the cup area in relation to the disc area in an individual patient. The test is easy to perform, takes little time and does not require dilation of the pupil. The main disadvantage is the high cost of the instrument, which makes it difficult for the individual ophthalmologist to own and operate one. It is hoped that, with time, the cost will become more manageable, and retinal tomography will become an essential part of the clinical work-up for optic nerve evaluation and monitoring.

Software is also available for estimation of retinal blood flow. At present these readings are not clinically reliable and not reproducible. Reliable retinal blood flow readings would be valuable to the clinician and no doubt this parameter and measurement will become more reliable in future generations of the software.

In retinal tomography the disc is green and the cup is red.

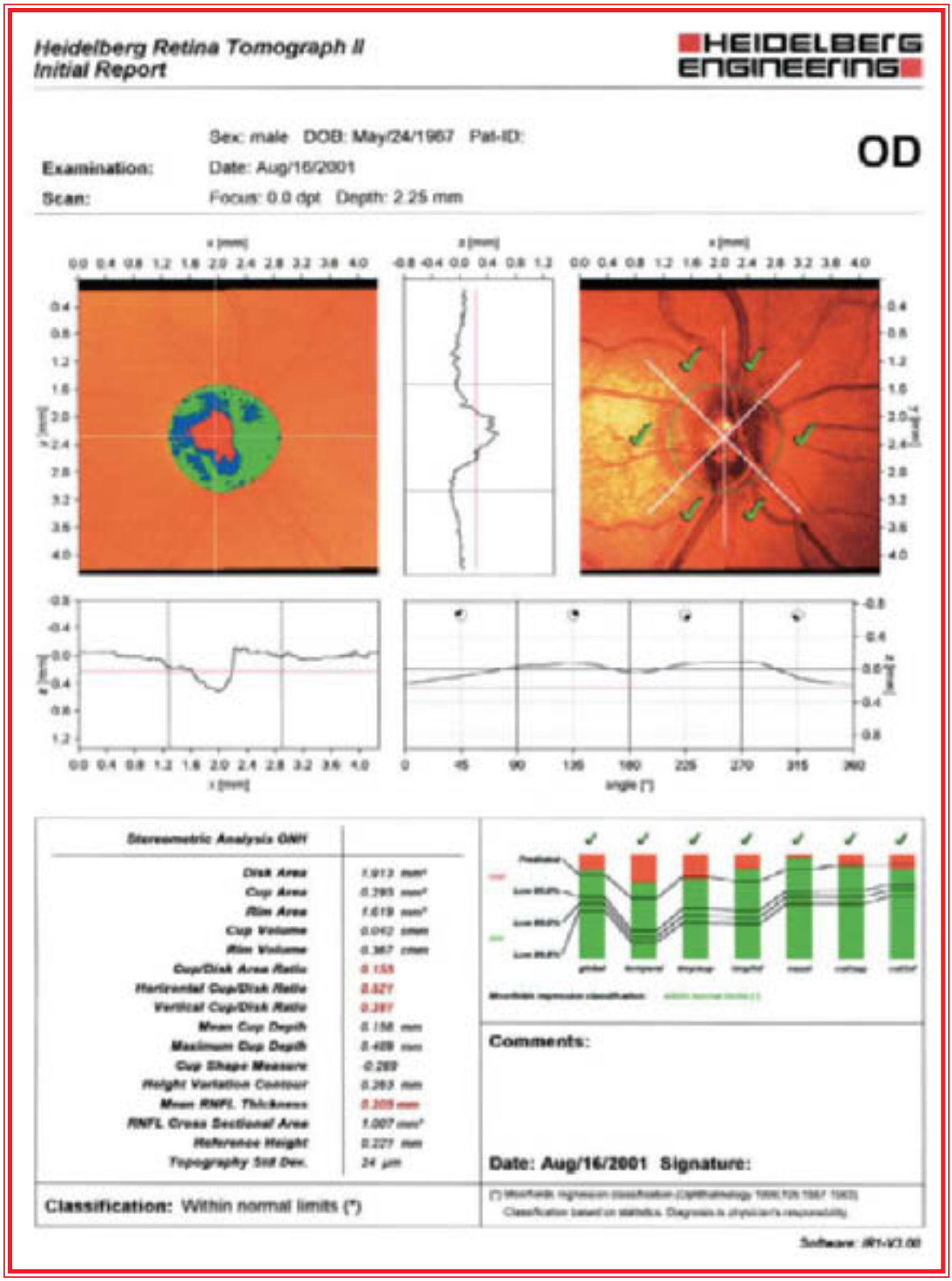


Figure 4A (Right Eye): Right and left eye retinal tomogram of patient with normal cup to disc ratios. The disc area is colored green the cup area is red. The retinal nerve fiber layer is of normal thickness, over 100 microns.

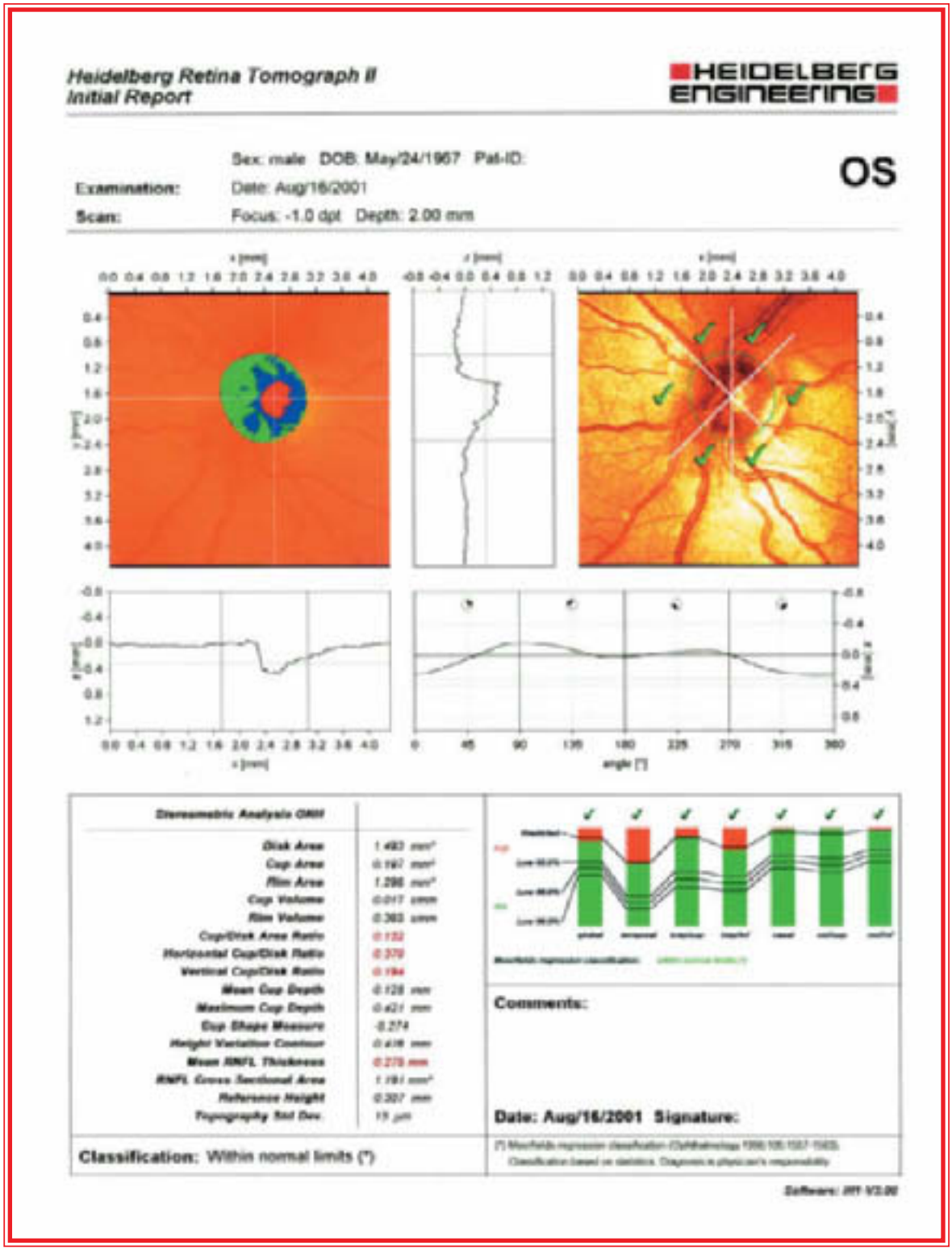


Figure 4B (Left Eye)

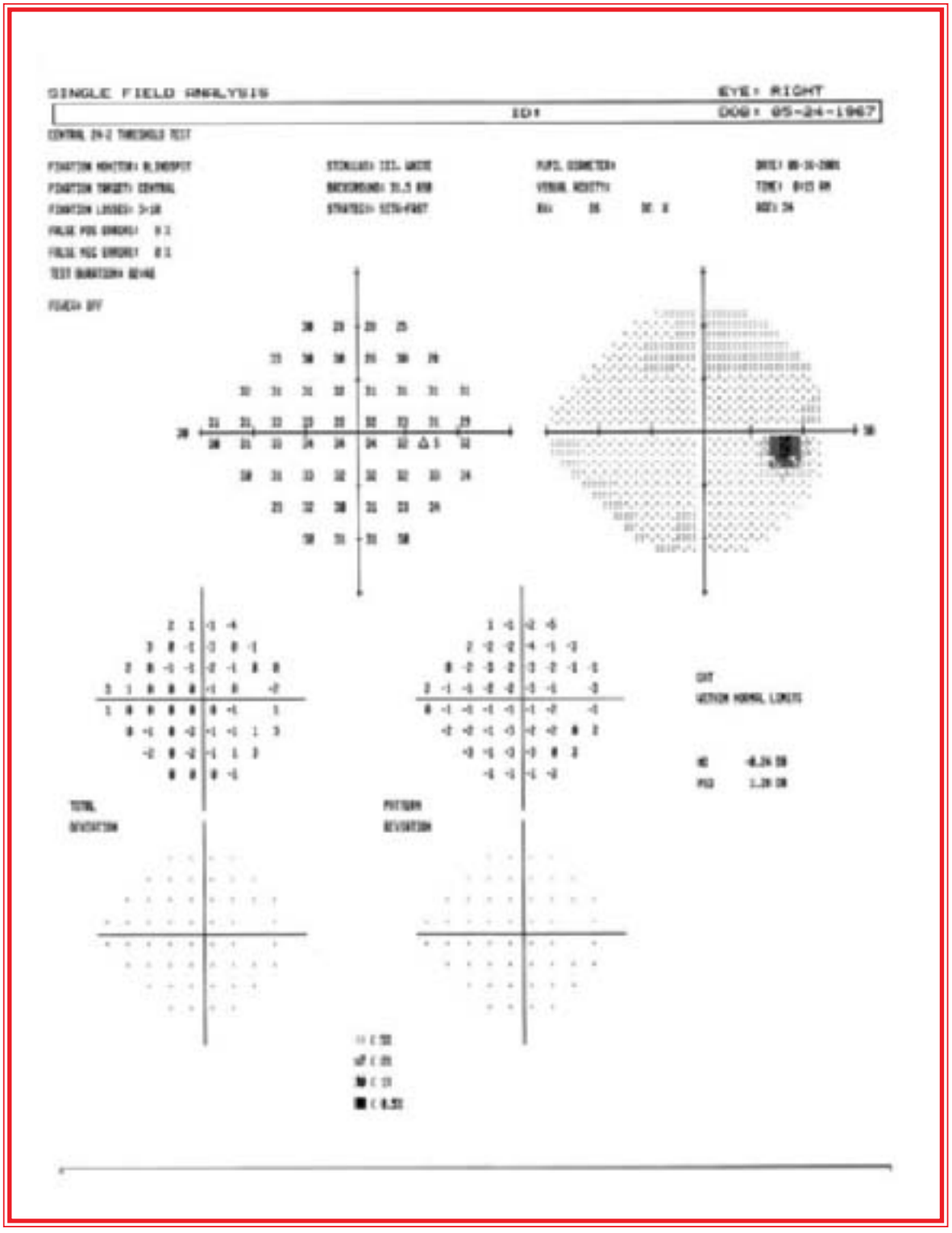


Figure 4C (Right Eye): Right and left Humphrey visual field of same patient from Fig. 4A-B The visual fields are normal.

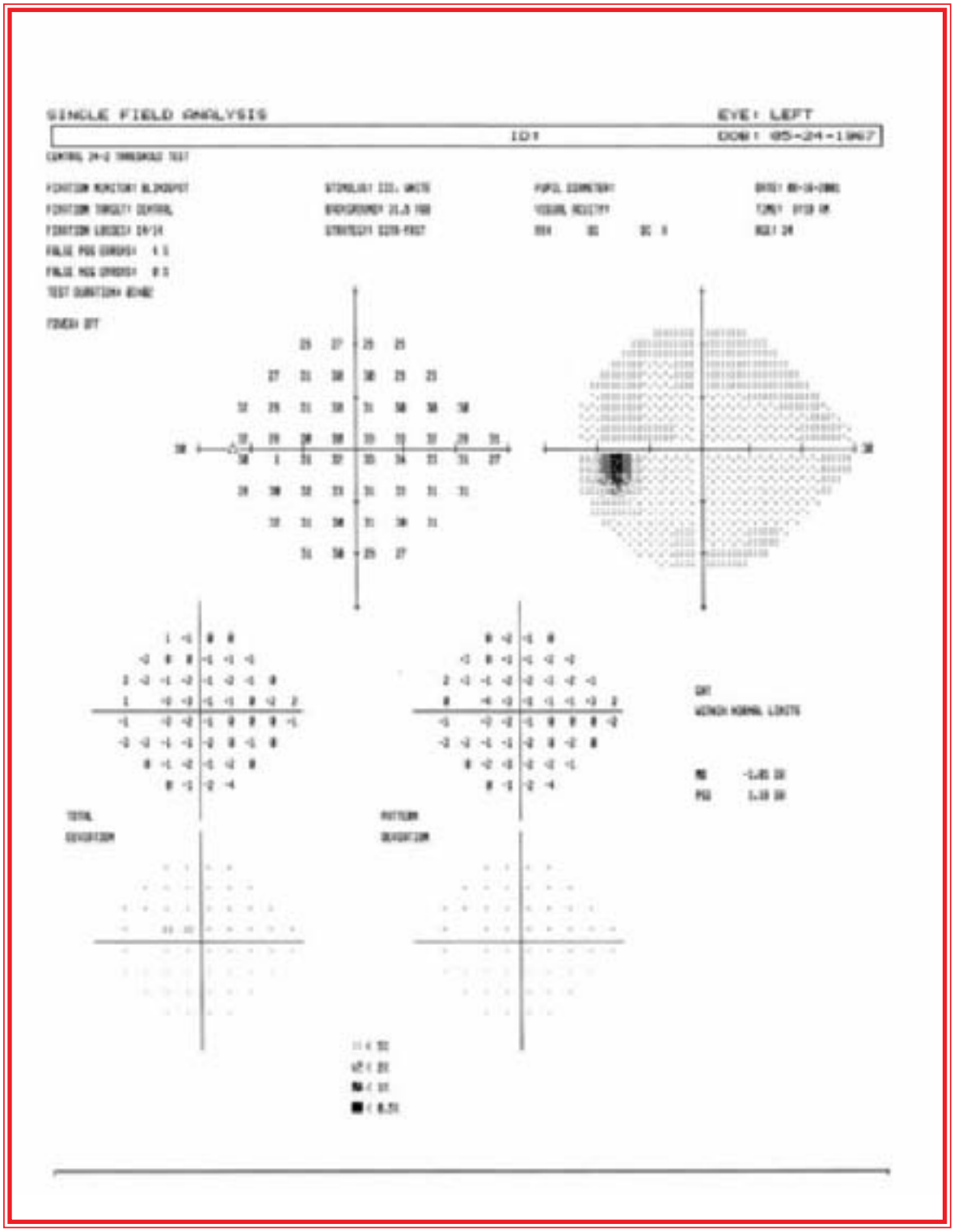


Figure 4D (Left Eye)

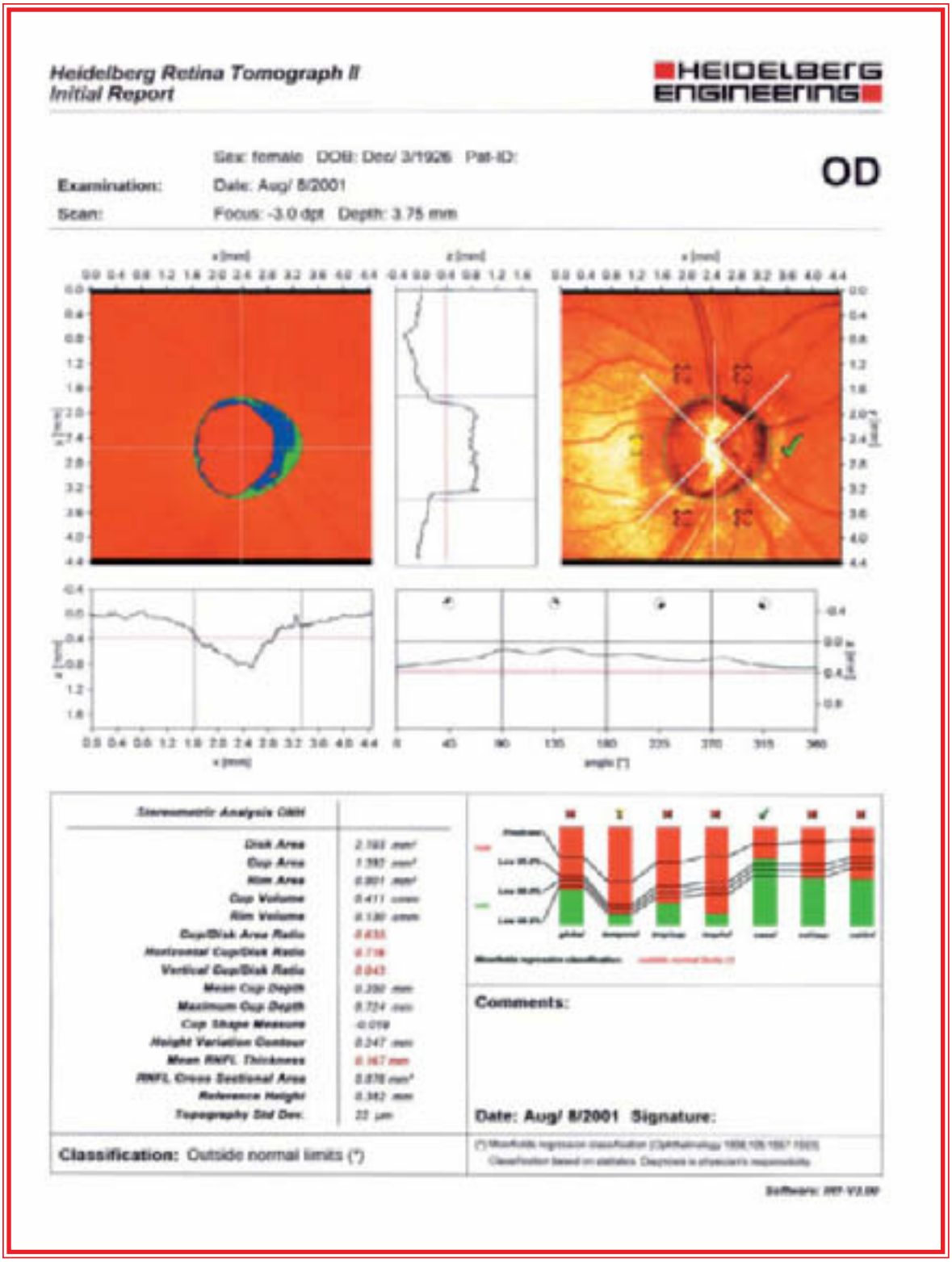


Figure 5A (Right Eye): Right and left retinal tomography of patient with cup disc ratios outside the normal (cup disc ratio >0.6). The nerve fiber layer (NFL) is not abnormally thin (the NFL measures over 100 microns) but the NFL is thinner in the eye with the larger cup disc ratio (right eye) as one would expect. Retinal tomography is not as accurate measuring NFL thickness as is OCT.

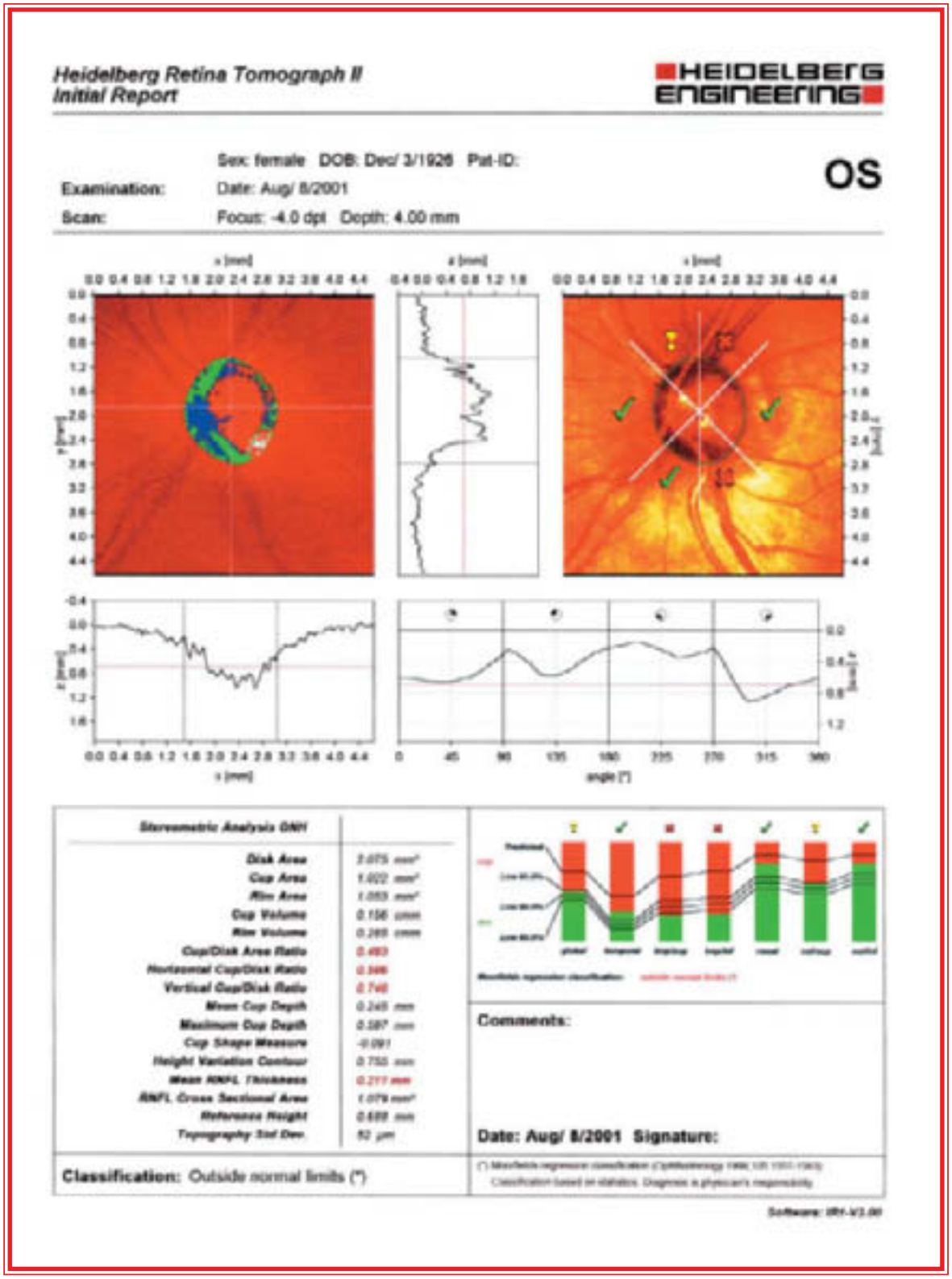


Figure 5B (Left Eye)

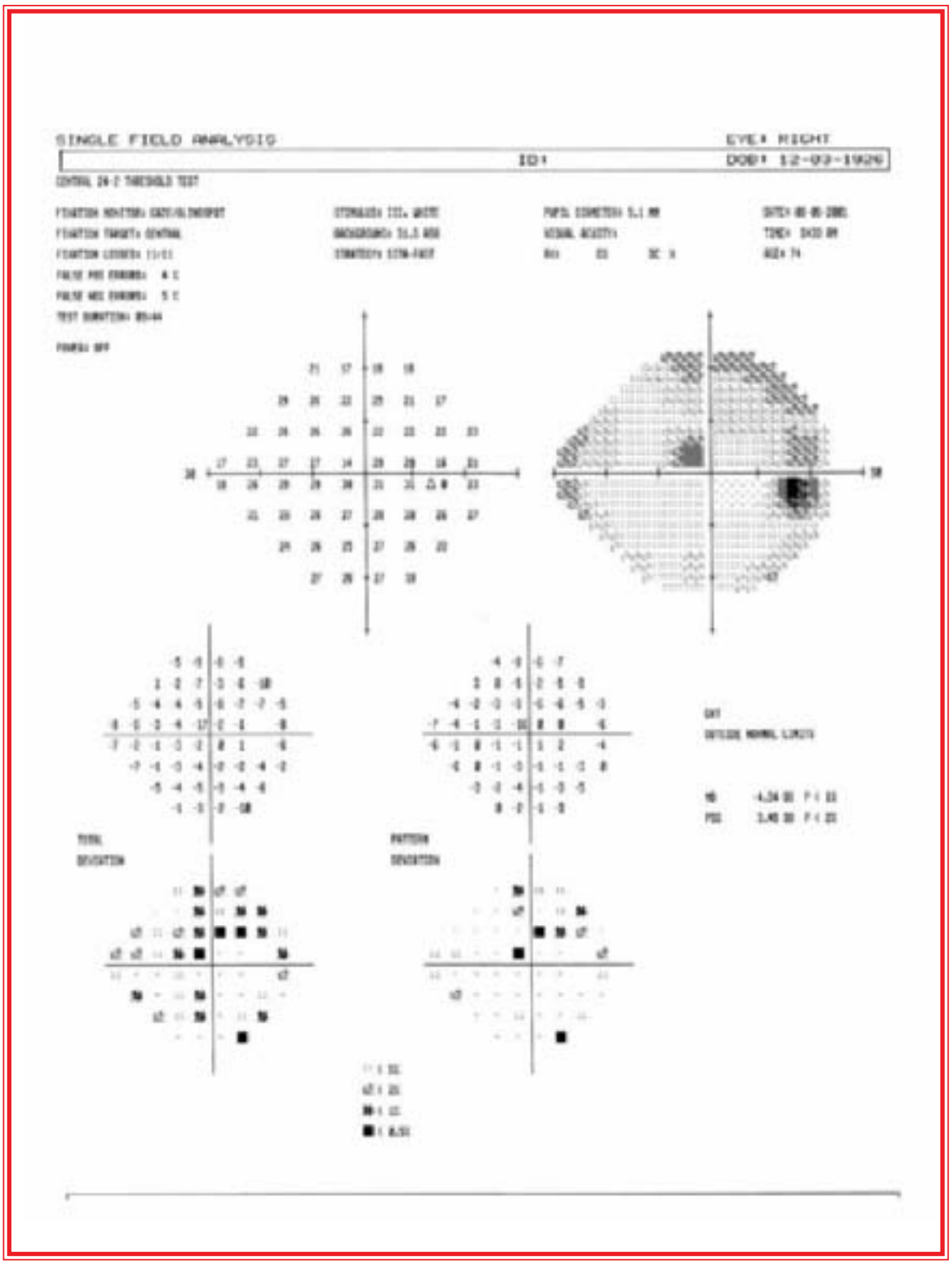


Figure 5C (Right Eye): Right and left Humphrey visual fields in same patient as Fig. 5A-B. The right eye has the larger cup disc ratio and a more extensive visual field defect. Both right and left visual fields are outside normal limits.

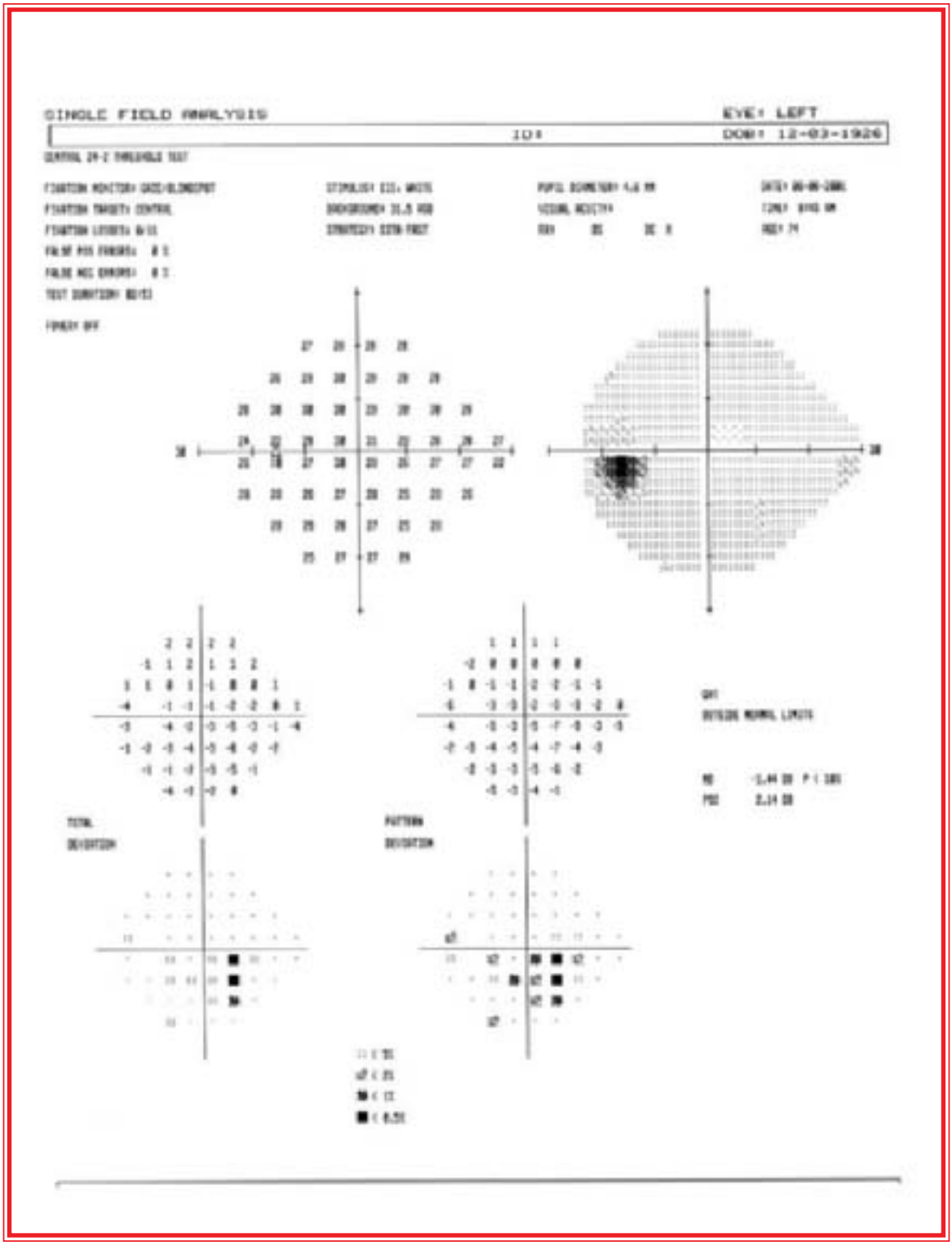


Figure 5D (Left Eye)

Suggested Readings

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Chapter 6
VHF ULTRASOUND IN THE EVALUATION OF GLAUCOMA

D. Jackson Coleman, M.D.

The advent of new transducer technology permitting very high frequency ultrasound evaluation of the anterior segment of the eye has permitted far more detail of this usually occult area of the eye to be imaged. This technology is a very useful adjunct in the evaluation of patients with glaucoma. Charles Pavlin who with Stuart Foster developed the first commercially available instrument for examination with frequencies in the very high frequency (VHF) 50 to 80 MHz range termed this technique Ultrasound Biomicroscopy, or UBM. This term is often used to refer to the commercial ultrasound instrument for VHF ultrasound examination. Our own VHF instrument, developed at Cornell University Medical College with the help of the Riverside Research Institute produces similar imaging quality but with a larger scan area (Figure 1) and with digital radio frequency data collection permits several computer derived analytical advantages including 3-D mapping, acoustic tissue typing (ATT), and scatterer pseudo-colorization. These images will be used to illustrate this article, demonstrating some uses of this technique, particularly in glaucomatous eyes.

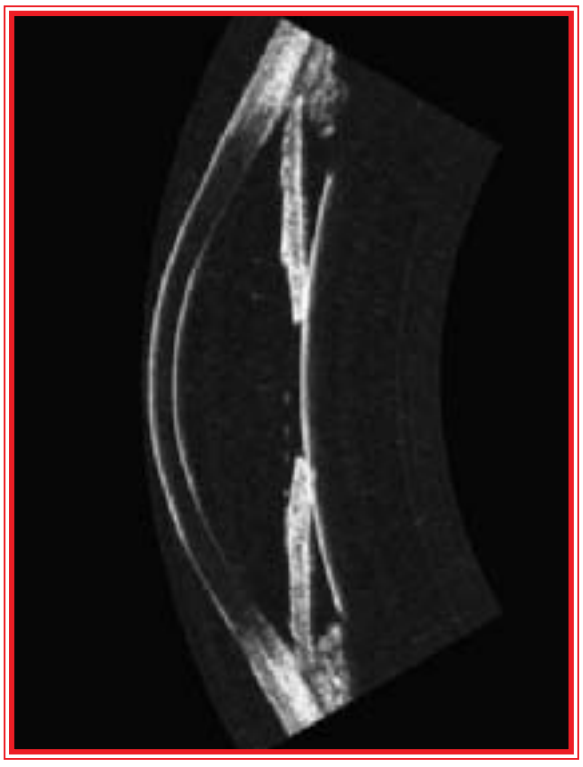


Figure 1 (Normal Arc):
VHF can show the dimensions of the anterior chamber both for corneal layers and anterior segment dimensions. Corneal layer measurement accuracy can approach 1 micron for thickness and the anterior segment can be measured to approximately 20 microns depending on the number of pixels used.

The anatomic features of ciliary body, iris and lens demonstrable at 50 MHz are normally imaged to a tissue depth of approximately 6mm, with higher frequencies giving better resolution but proportionately less depth of assessment. For example, at 100 MHz only about 2mm depth can be imaged. With VHF, the iris can be imaged well with particularly good reflectivity from the melanin in the pigment epithelium. The angle can be visualized and Schlemm's Canal usually defined (Figure 2). Anatomic conditions such as plateau iris (Figure 3) and iris concavity or variation in pigmentary glauco-

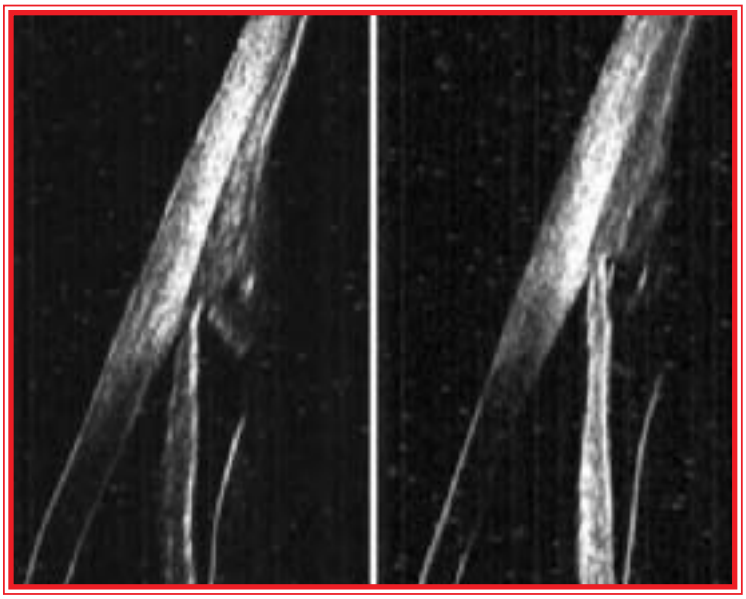


Figure 2 (Normal Angle):
The ciliary body is shown with iris, angle and overlying sclera and cornea with excellent anatomic detail. It must be remembered that the image in all B-scan ultrasound is anamorphic in that the dimension along the ultrasound path depends on sound velocity while the orthogonal axis is dependent on beam movement and geometry.

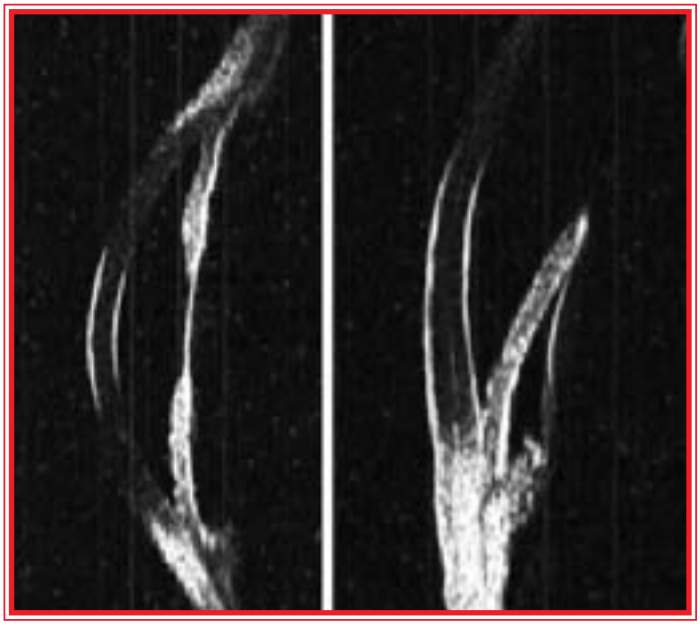


Figure 3 (Plateau Iris):
In plateau iris, the relation of iris to ciliary body and lens as well as corneo-scleral angle can be shown and the ciliary processes demonstrated as anteriorly placed. A larger area of contact between lens capsule and iris are demonstrated in the figure on the left.

ma (Figure 4) are demonstrable and the effects of exercise, drugs, light or surgery can be assessed. Pupillary block (Figure 5) is seen as a forward bowing of the iris, adhesion or cystic causalities can be identified. Surgical efficacy can be demonstrated for iridotomy as well as filtering procedures (Figure 6),

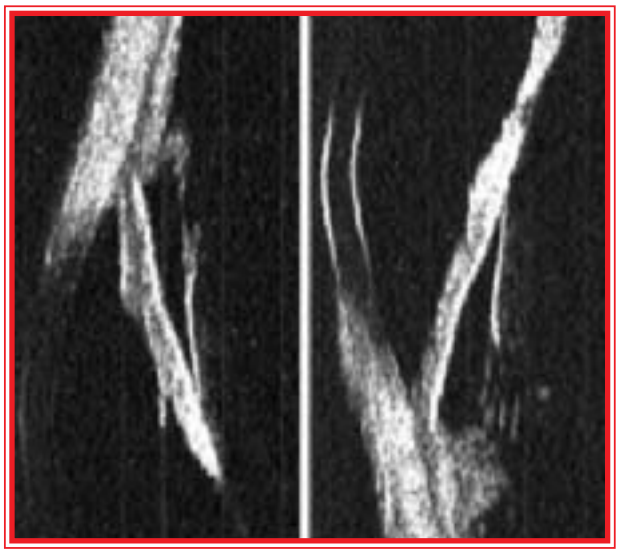


Figure 4 (Pigmentary Glaucoma):
The iris in pigmentary glaucoma shows flexibility on successive scans and the deposition of pigment on the zonule can enhance zonular imaging with VHF ultrasound.



Figure 5 (Pupillary Block):
In pupillary block glaucoma, a forward bowing of the iris with adhesions to the lens can easily be seen and the retro-iridal area clearly identified for other possible pathology.



Figure 6 (Bleb):
VHF scans of a filtering bleb will show the bleb space as well as possible anatomic changes of underlying sclera which may include hypotonous changes of separation of the ciliary body from the sclera as is shown in this figure (arrow).

and complications such as persistent hypotony (Figure 7) can be evaluated for possible separation of the ciliary body from the sclera. The position and degree of separation as well as possible irido- or vitreo-ciliary traction can be demonstrated as well, aiding in surgical management. Surgical intervention such as Molteno tube (Figure 8) placement can be clearly defined with serial B-scans. Traumatic changes such as foreign bodies (Figure 9), or surgically induced changes such as intraocular lens place-



Figure 7 (Hypotony):
In this figure hypotony is clearly demonstrated due to a separation of the ciliary body from the sclera. Different forms of traction, such as 1) vitreo-ciliary or iridal-ciliary membranes, or 2) irido-ciliary dialysis or 3) scleral perforation can be identified.



Figure 8 (Molteno Tube):
A Molteno tube placed in the anterior chamber and into the subconjunctival space can be mapped and its location identified even when conventional visualization techniques are inadequate.

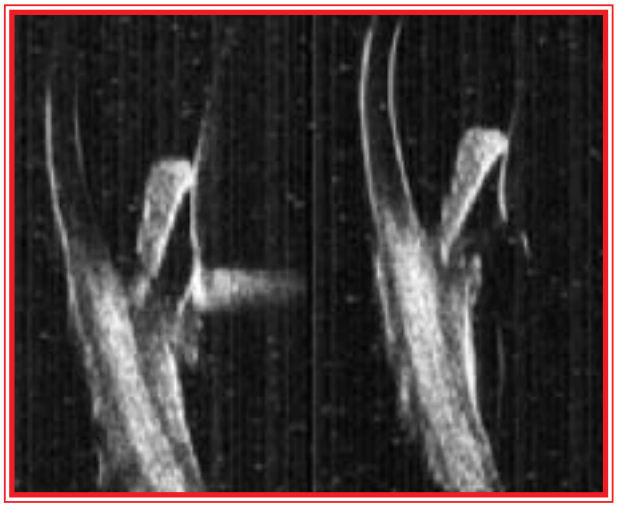


Figure 9 (Foreign Body):
An intraocular foreign body resting on the lens equator can be seen while an adjacent scan shows normal appearing ciliary and lens anatomy. This serial section is helpful not only in locating foreign bodies in this occult region but in demonstrating relative size by evaluating scan separation.

ment, can be studied. The position of the haptics, which can be a major source of persistent complications, whether eroding into the ciliary body, producing pain or hemorrhage, or folded back on the iris, creating a pigmentary glaucoma, can be identified and treated (Figure 10).

Computer assisted three dimensional reconstruction can be of further aid in demonstrating the degree and type of anatomic variation. With reconstruction techniques, areas of tissue or foreign body continuity can be colorized to permit true 3-dimensional perspective and assessment.

Iris and ciliary body tumors (Figure 11) and simulating lesions such as cysts (Figure 12) or lens remnants can be nicely resolved with VHF. Patients can be followed for tumor regression following radi-

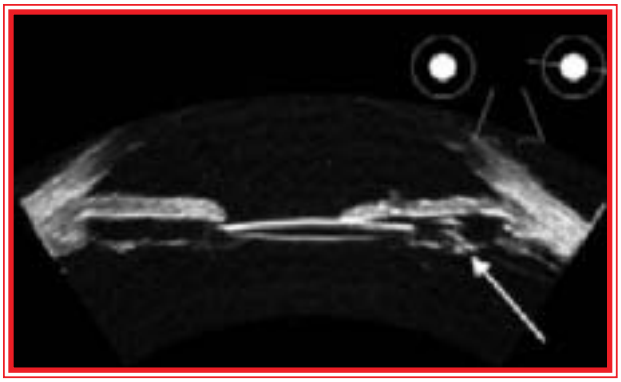


Figure 10 (Pigmentary Glaucoma):
This figure shows an intraocular lens with an extruded soft haptic that is folded over (arrow). This not only allowed the lens to displace towards the haptic, but for the lens to rub off pigment, creating pigmentary glaucoma.

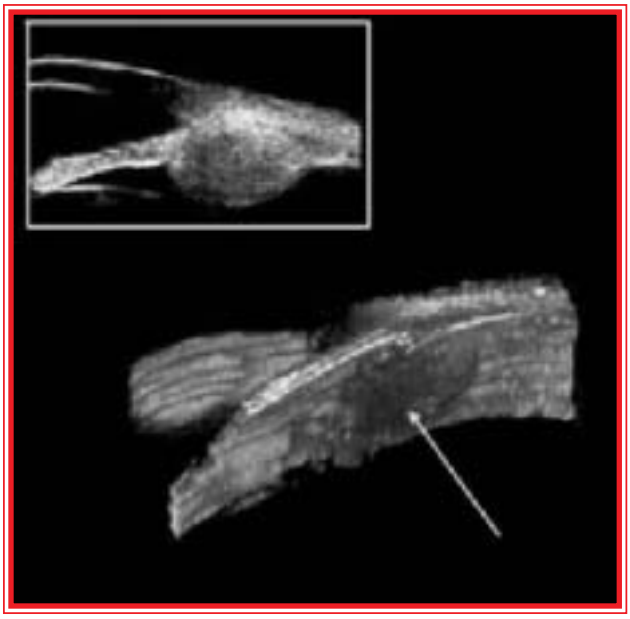


Figure 11 (3-D Tumor):
A ciliary body tumor is shown on a single section (upper left) with 3-D presentation in the lower right (arrow). Tumor volume can be accurately measured to within approximately 4%. Tumor typing can be performed, and scatterer concentrations can be used to monitor the effects of brachytherapy and/or hyperthermia.

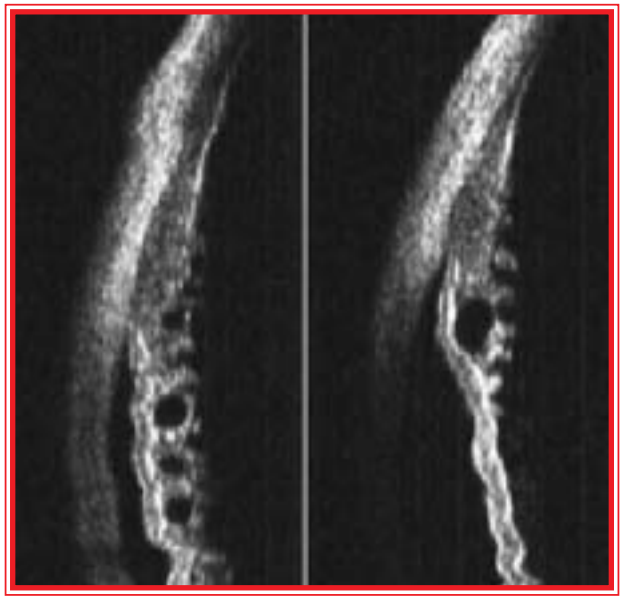


Fig 12 (Ciliary Cyst):
Cystic changes which can mimic a ciliary body tumor can be easily identified and followed for possible progressive change.

ation by mapping the scatterer concentration and location.

Similarly, computer generated and identifiable sub-resolvable properties of tissue features can be used to identify tissue changes seen in the ciliary body due to the effect of pharmacologic agents such as miotics and mydriatics (Figure 13). Vascular flow in small vessels and capillaries are areas of present investigation in order to further study pharmacologic and ischemic disease induced effects on the ciliary body.

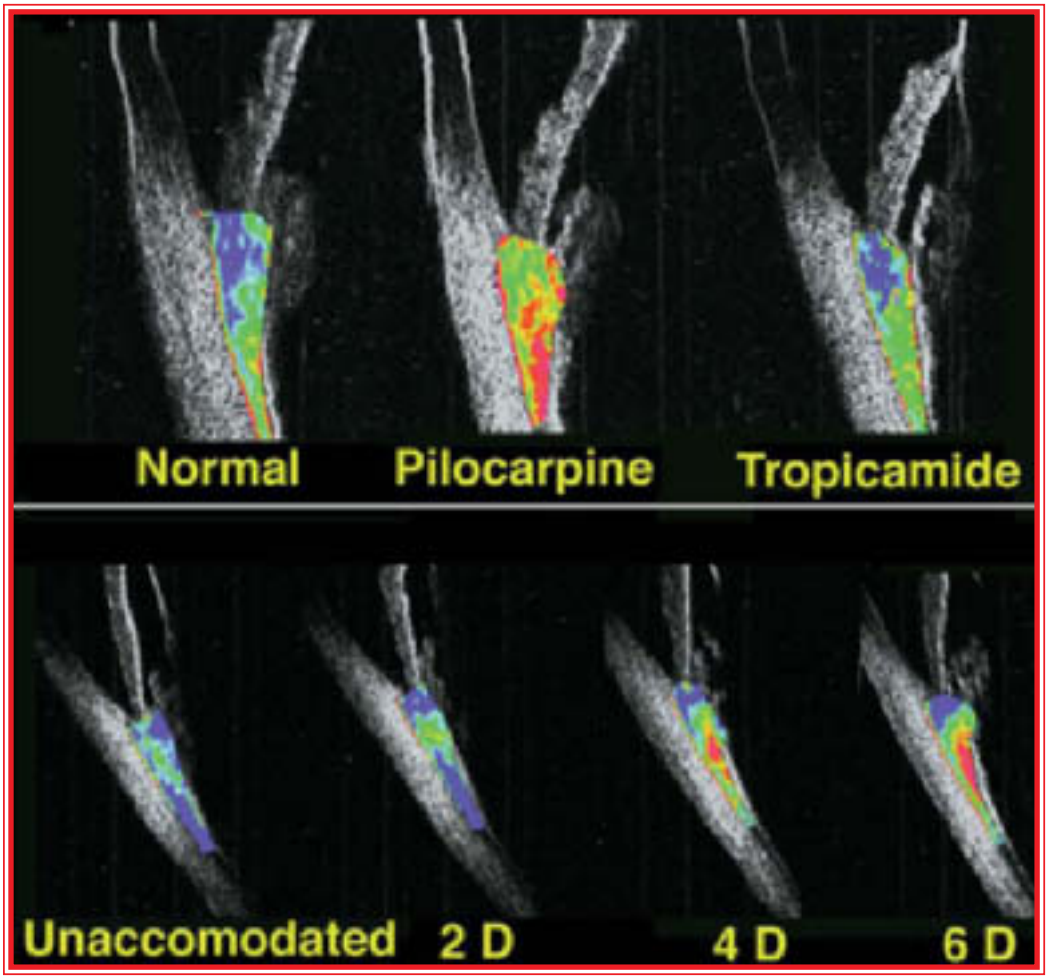


Figure 13 (Pseudo-Color):
Identification of scatterers in the ciliary body and mapping through pseudo-color animation allows the effects of pharmacologic agents or physiologic effects such as accommodation, or temporal changes such as aging to be studied.

Chapter 7
GENETIC TESTING AND A MOLECULAR PERSPECTIVE ON GLAUCOMA
New Insights Into Understanding Mechanisms of Glaucoma

Andrea Vincent, M.D.
Elise Heon, M.D.
Graham Trope, M.D.

Glaucoma's hereditary aspects were recognized more than 150 years ago[1-3] but only in the last decade has it been used as a tool to better understand the molecular basis of the disease. Determining the genetic basis of glaucoma has been more difficult than anticipated, but it is providing new insights into the underlying mechanisms. The difficulties are due to the fact that many glaucoma genes are involved (genetic heterogeneity) and the clinical features distinguishing them can be subtle and show some overlap (variable expression). However, molecular diagnosis will soon become an avenue for earlier diagnosis and improved management of the disease.

This article highlights the recent advances in genetic research of glaucoma and demonstrates the implication of these discoveries for the potential management of glaucoma patients.

As molecular information accumulates, a new nomenclature is being developed and a new classification of glaucoma is proposed (Table 1). The label 'GLC1' refers to open angle disorders, 'GLC2' refers to closed angle glaucoma and 'GLC3' refers to congenital forms of glaucoma. Each new 'genetic subset' characterized is designated in the alphabetical order in which they are identified. For example, 'GLC1A' refers to the open angle glaucoma mapped to chromosome 1q25, often referred to as juvenile open angle glaucoma (see below).

Juvenile and Primary Open Angle Glaucoma (JOAG and POAG)

Juvenile open angle glaucoma (JOAG) has been a major point of focus of glaucoma genetic research in recent years because the inheritance pattern was known and families affected with the disease were available to study. The early age of onset of this condition and its dominant inheritance has helped with the identification of the first open angle glaucoma gene (MYOC).

In 1993, Sheffield et al identified the first genetic location (locus) of a JOAG gene in a study of a large North American family affected with juvenile glaucoma[4]. This locus, now referred to as GLC1A, has been confirmed by many groups to be associated with an open angle glaucoma phenotype of variable age of onset (variable expression)[5-8]. In 1997,

Table 1. Genetic Classification of Glaucoma

Glaucoma Type	Locus	Location	Gene
Primary Open Angle Glaucoma			
Conventional Designation	***Molecular Designation***		
JOAG	GLC1A	1q23-25	***MYOC***
POAG (partly normal tension)	GLC1B	2cen-q13	N/A
POAG	GLC1C	3q21-24	N/A
POAG	GLC1D	8q23	N/A
POAG (normal tension)	GLC1E	10p15-p14	N/A
POAG	GLC1F	7q35-36	N/A
Congenital Glaucoma			
PCG	GLC3A	2p21	***CYP1B1***
PCG	GLC3B	1p36	N/A
Associated Developmental Anomalies			
Axenfeld-Rieger sd, iris hypoplasia, iridigoniodysgenesis	RIEG1/IRID2	4q25	***PITX2***
Rieger syndrome	RIEG2	13q14	N/A
Axenfeld-Rieger sd, iris hypoplasia	IRID1	6p25	***FOXC1***
Iridogoniodysgenesis syndrome	IRID1	6p25	N/A
Anterior segment dysgenesis		10q25	***PITX3***
Anterior segment dysgenesis		20p11-q11	***VSX1***
Anterior segment dysgenesis		1p32	***FOXE3***
Aniridia/Congenital glaucoma		11p13	***PAX6***
Other Loci			
PDS/Pigmentary Glaucoma	GPDS1	7q35-36	N/A
PDS/Pigmentary Glaucoma	GPDS2	18q11-21	N/A
Nanophthalmos/Angle closure	NNO1	11	N/A
Cornea plana/Angle closure		12q21	N/A
Nail-Patella syndrome	NPS1	9q34	***LMX1B***
PPMD	PPMD	20q11-p11	N/A
CHED	CHED	20q11-p11	N/A

Legend:
PPMD: Posterior Polymorphous Dystrophy
CHED: Congenital Hereditary Endothelial Dystrophy

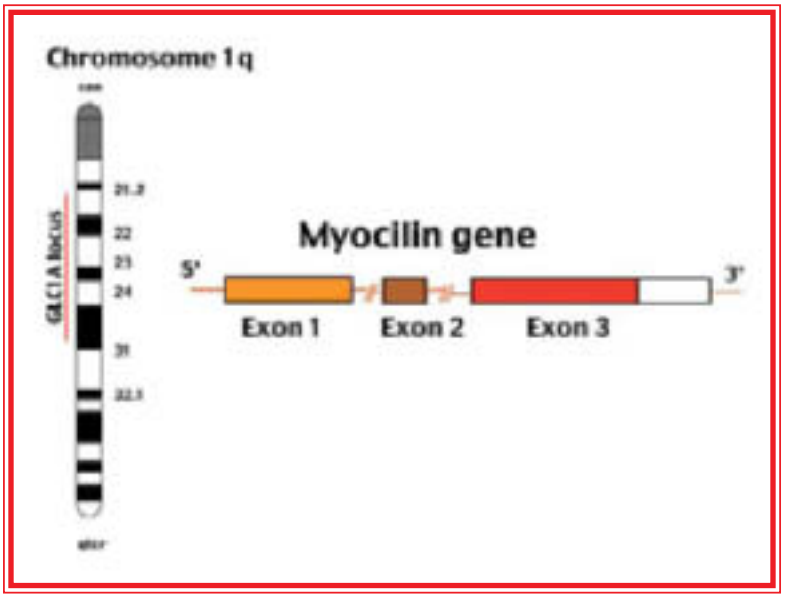


Figure 1.
Ideogram of chromosome 1 with localization of MYOC. MYOC has 3 exons with mutations concentrated in exons 1 and 3.

Stone et al identified mutations in the myocilin gene (gene symbol MYOC) at the GLC1A locus (Figure1) in patients with JOAG[9]. The myocilin protein was first identified in trabecular meshwork cells when high levels of both mRNA and protein were induced by dexamethasone administration[10], therefore this gene was initially called TIGR (Trabecular meshwork-Induced-Glucocorticoid-Response protein). The name Myocilin was chosen by the Human Genome Committee to refer to this glaucoma gene at the GLC1A locus, so the term TIGR has been dropped.

In normal eyes MYOC mRNA is expressed in the iris, ciliary body and trabecular meshwork [11-13], as well as the retinal photoreceptor cells[14] and optic nerve head[15]. Despite an intensive research effort, the biological significance of mutant myocilin protein and its role in the pathophysiology of glaucoma is unclear. One theory is that impairment of outflow occurs at the level of the trabecular meshwork. Support for this is demonstrated by perfusing the trabecular meshwork with mutant recombinant protein, resulting in an increase in outflow resistance[16], and mutant myocilin proteins have reduced solubility in-vitro compared with normal protein[17]. The real cause of glaucoma-related visual function loss in these cases however remains to be defined.

Recent studies estimate that MYOC mutations are found in 3.4 - 5% of sporadic adult-onset open angle glaucoma and 8 - 10% of familial JOAG cases[18-21]. A large study of 1703 glaucoma patients from 5 different populations showed the overall frequency of myocilin mutations (2-4%) to be similar in all populations[19].

The variable expressivity of GLC1A-related phenotypes is significant and can range from juvenile glaucoma to typical late-onset POAG, associated with a variable degree of severity, rate of progression and intraocular pressure (IOP). This variable expression of MYOC, which can be observed within a family, is influenced by factors not yet identified. Certain MYOC mutations are associated with a characteristic clinical picture (phenotype-genotype correlation). An example is the Gln368Stop mutation, the most common mutation in all populations, which is associated with an older age of onset and less elevation of IOP than the Pro370Leu mutation, which is usually associated with disease onset before the age of 20 years, and an average IOP of 45mmHg. The ultimate aim of this work is to eventually design therapeutic trials targeting specific MYOC mutations to optimize the treatment.

As MYOC mutations are identified in only 8-10% of the familial cases with JOAG, this suggests genetic heterogeneity; i.e. similar phenotypes have

different underlying genetic causes. Some pedigrees with autosomal dominant JOAG have not been linked to the GLC1A locus, or to other of the known glaucoma loci[22,23]. These findings imply more JOAG genes are to be identified.

Adult-Onset Primary Open Angle Glaucoma

Adult-onset primary open angle glaucoma (POAG or COAG), the most common form of glaucoma, tends to have a later onset and less aggressive disease progression than what is seen in JOAG. However, genetic studies have shown that POAG and JOAG are not truly two distinct diseases as in some cases they share a common underlying genetic defect. As discussed, some autosomal dominant JOAG pedigrees linked to the GLC1A locus contain individuals with a typical POAG phenotype.

The prevalence of MYOC mutations in a POAG population (3.4 - 5%), coupled with the prevalence of glaucoma in the general population, suggests mutations in the GLC1A gene could cause glaucoma in over one hundred thousand North Americans. This would make GLC1A-related glaucoma one of the most recognizable forms of blindness.[9]

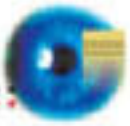
There is now compelling evidence indicating that several other genes contribute to POAG. Other loci have been identified for POAG on chromosome 2cen-q13(GLC1B), 3q21-q24 (GLC1C), 8q23 (GLC1D), 10p15-p14 (GLC1E), and 7q35-36 (GLC1F) 20 (Table 1). Variable phenotypes are also associated with these loci. Several families which provided linkage to the GLC1B locus were characterized by a normal to moderate pressure glaucoma manifesting in the 5th decade[24]. The large American family linked to GLC1C had glaucoma characterized by a diagnosis before the age of 50, IOPs in the mid-20's, and associated glaucomatous optic nerve and / or visual field changes[25]. The GLC1D phenotype shows variable severity whereas the GLC1E was associated with normal tension glaucoma. GLC1F glaucoma appears to be the common POAG variant. Therefore High and Low tension POAG show genetic heterogeneity. Identification of the GLC1B-F genes will provide an opportunity for detection of at-risk individuals permitting optimal use of current therapies and a better understanding of the underlying disease process.

Although large families affected with POAG are difficult to recruit, heredity is clearly documented and a different approach using sibpairs of affected individuals is being successful in identifying new glaucoma loci. The downside to this approach is that it requires a very large number of sibpairs for the genome-wide screen to find statistical significance. This approach has recently highlighted potential loci on chromosomes 2, 14, 17p, 17q and 19[26].

In order for these genes to be identified, more families with a genetic history of glaucoma need to be recruited and analyzed. The opportunity now exists for the clinician to contribute to the identification of more glaucoma genes by identifying large families and sharing them with scientists involved in this type of research.

Other forms of Open Angle Glaucoma

Nail-patella syndrome is a rare autosomal dominant disorder characterized by a variable degree of dysplasia of the nails and bones which has been associated with open angle glaucoma in 31% of cases



studied. The age of onset of these cases was highly variable ranging between 18 years and 40 years. After linkage of 2 pedigrees to chromosome 9q34, mutations in the LMX1B gene, a transcription factor, were found segregating with this disease in 4 families[27,28]. The role of LIMX1B in isolated POAG demands further investigation.

There is also evidence for a genetic contribution to pseudoexfoliative glaucoma, with documentation of maternal transmission in some pedigrees[29] but a genetic locus is yet to be identified.

Pigmentary Dispersion Syndrome and Pigmentary Glaucoma

Family studies suggest that a dominant hereditary factor plays a role in pigmentary glaucoma and/or pigment dispersion syndrome (PDS) [30,31]. Twenty to fifty percent of individuals with PDS are at risk of developing glaucoma[32,33]. Even though the variable expressivity of this condition makes familial studies difficult, the linkage analysis of affected pedigrees has excluded the role of MYOC in PDS 23,34. Two loci for PDS were mapped to 7q35-q36 in 4 autosomally dominant affected pedigrees[35], and to 18q11-21[36] (Table 1). Although a mouse model for PDS has been developed [37,38] and a locus identified (ipd), mutations have not yet been demonstrated in a gene. Analysis of more families will help better define the human loci identified and the extent of the genetic heterogeneity of this disease. Further molecular testing for this condition is needed, especially in large families.

Implications

The importance of identifying individuals at risk of developing glaucoma before optic nerve damage occurs cannot be over-emphasized, as this damage is most often irreversible. Analysis of the MYOC gene is a first step in the identification of those at risk of developing this form of glaucoma-related visual loss. This genetic approach will allow selective follow-up of those at risk of developing the disease and earlier introduction of tailored therapy.

Congenital Glaucoma

Patients with congenital glaucoma usually present during the first year of life often with the classic clinical triad of epiphora, blepharospasm and photophobia. Bilateral corneal edema and Haab's striae are typical findings related to the increased intraocular pressure. Megalocornea and buphthalmos can develop if the pressure is not controlled [39]. When hereditary, the inheritance pattern is usually autosomal recessive. Several chromosomal anomalies have been associated with this condition[40] but it was only recently that the first congenital glaucoma-related genes were localized. Sarfarazi et al (1995) studied 17 families from Turkey and Canada with autosomal recessive congenital glaucoma[41] and identified the first congenital glaucoma disease locus on chromosome 2p21 (GLC3A). The suspected genetic heterogeneity of primary congenital glaucoma (PCG) was confirmed by identification of a second locus on chromosome 1p36 (GLC3B)[42]. Some families remain unlinked, which suggest that a third congenital glaucoma locus is yet to be identified (Table 1).

The gene responsible for the glaucoma at the GLC3A locus, CYP1B1 (Figure 2), is now available for mutational analysis. CYP1B1 encodes a protein that is a member of the cytochrome P450 enzyme family. Mutations were initially demonstrated in this gene co-segregating with autosomal recessive PCG accounting for up to 85% of the disease in consanguineous communities[43-48]. However, in other more ethnically mixed populations only 20- 30% of PCG cases are attributable to CYP1B1 mutations, which is still a significant subset of the disease[49], [50]. Incomplete penetrance and variable expression have also been documented[44]. This implies that an individual with the genetic defect may not develop the disease or may develop it later. However the risk of transmitting the genetic defect is unchanged. These findings support the importance of examining families of affected individuals with congenital glaucoma.

Recently mutations in CYP1B1 have been identified in patients with Peters anomaly which confirms the role of this gene in anterior segment development[51]. The specific role of this gene is yet to be elucidated as the substrate that it acts on in the eye is not yet identified, although it is known to play a role in steroid metabolism by catalyzing 17-b-estradiol. Future studies will allow better counseling of patients and a clearer understanding of the fundamental mechanisms involved in this form of glaucoma-related visual loss.

Developmental Glaucoma

Anterior segment developmental anomalies have a strong association with glaucoma and encompass a wide spectrum of clinical findings. These include the variable clinical manifestations of Axenfeld-Rieger syndrome[52] with iris hypoplasia, iridogoniodysgenesis, associated maxillary, dental and umbilical abnormalities and various less specific clinical variants of anterior segment dysgenesis. Mutations in one of the known developmental eye genes PITX2, FOXC1 or PITX3 may manifest with

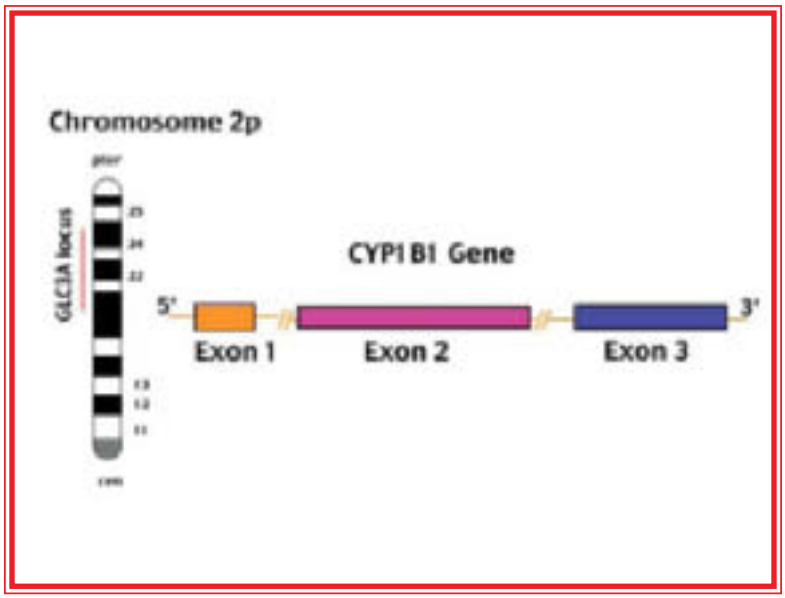


Figure 2.
Ideogram of chromosome 2 with localization of CYP1B1. Exons 2 and 3 are the only coding portion of this gene.

Table 2. Genotype-Phenotype Correlation

Gene	Associated Phenotypes
MYOC	JOAG, POAG
CYP1B1	Congenital Glaucoma, Peters anomaly
PITX2	Iris hypoplasia. Rieger syndrome, Iridogoniodysgenesis
PITX3	Anterior segment dysgenesis
VSX1	Anterior segment dysgenesis
FOXC1	Iris hypoplasia. Rieger syndrome, Iridogoniodysgenesis, Peters' anomaly
FOXE3	Anterior segment dysgenesis/ cataracts
PAX6	Aniridia, Foveal hypoplasia, Peters' anomaly, Keratitis, Congenital glaucoma

similar, yet variable clinical phenotypes (Table 2). In other terms there is a significant degree of phenotypic overlap among the various genetic subtypes.

Linkage analysis of pedigrees with Rieger Syndrome to a locus on 4q25 (RIEG1)[53], lead to the identification of the PITX2 gene (previously called RIEG). PITX2 is a homeobox transcription factor that belongs to a family of genes involved in developmental regulation of tissue expression. A common feature associated with mutations in this gene is abnormal development of the anterior segment of the eye. The spectrum of PITX2 expression ranges from subtle iris hypoplasia, Axenfeld-Rieger syndrome and Peter's anomaly[54-58].

Another locus was mapped to chromosome 6p25 (IRID1) from the study of pedigrees affected with iridogoniodysgenesis with and without glaucoma and Axenfeld-Rieger syndrome [59-61]. Mutations and duplications of FOXC1, another transcription factor gene within this locus, (previous nomenclature FKHL7 – forkhead/winged-helix like), have now been demonstrated to cause Axenfeld-Rieger anomaly, iris hypoplasia, Peters anomaly and Rieger syndrome at 6p25[62-65]. Some pedigrees have been linked to 6p25 but do not have mutations in FOXC1, suggesting a second gene at this locus[60,62]. Recent evidence of duplications at this locus warrants further investigation of these pedigrees.

Mutations in 4 other genes encoding transcription factors have also been found in pedigrees with anterior segment dysgenesis. These genes are PITX3 (10q25)[66], VSX1 (20p11-q11)[67], FOXE3 (1p32)[68], and PAX6 (6p11-13)[69]. The phenotype variability associated with these genes is important and beyond the scope of this paper. It is anticipated that further loci will be found in association with this already genetically heterogeneous group of disorders. Further characterization of the action of the genes involved in anterior segment developmental abnormalities should provide greater insight into the mechanisms of glaucoma in this population.

Angle-closure Glaucoma

A large pedigree affected with nanophthalmos and angle-closure glaucoma linked to chromosome 11 (NNO1)[70], and a further pedigree with angle-closure glaucoma associated with cornea plana mapped to 12q21[71]. Future identification of the genes involved may allow examination of the relationship between these entities and sporadic angle-closure glaucoma.

Conclusion

Despite therapeutic advances, glaucoma remains a leading cause of permanent blindness worldwide. A major difficulty in management of this condition resides in early diagnosis before the condition leads to irreversible optic nerve and visual function damage. The genetic approach to the study of glaucoma has currently identified at least eighteen glaucoma-related loci (Table 1). The identification of an increasing list of glaucoma-related genes allows us to now identify a number of those at risk of developing the disease and direct them towards earlier sight-saving therapy. The identification of more genes and the elucidation of the molecular pathway will likely lead to the development of novel therapies and sight saving approaches.

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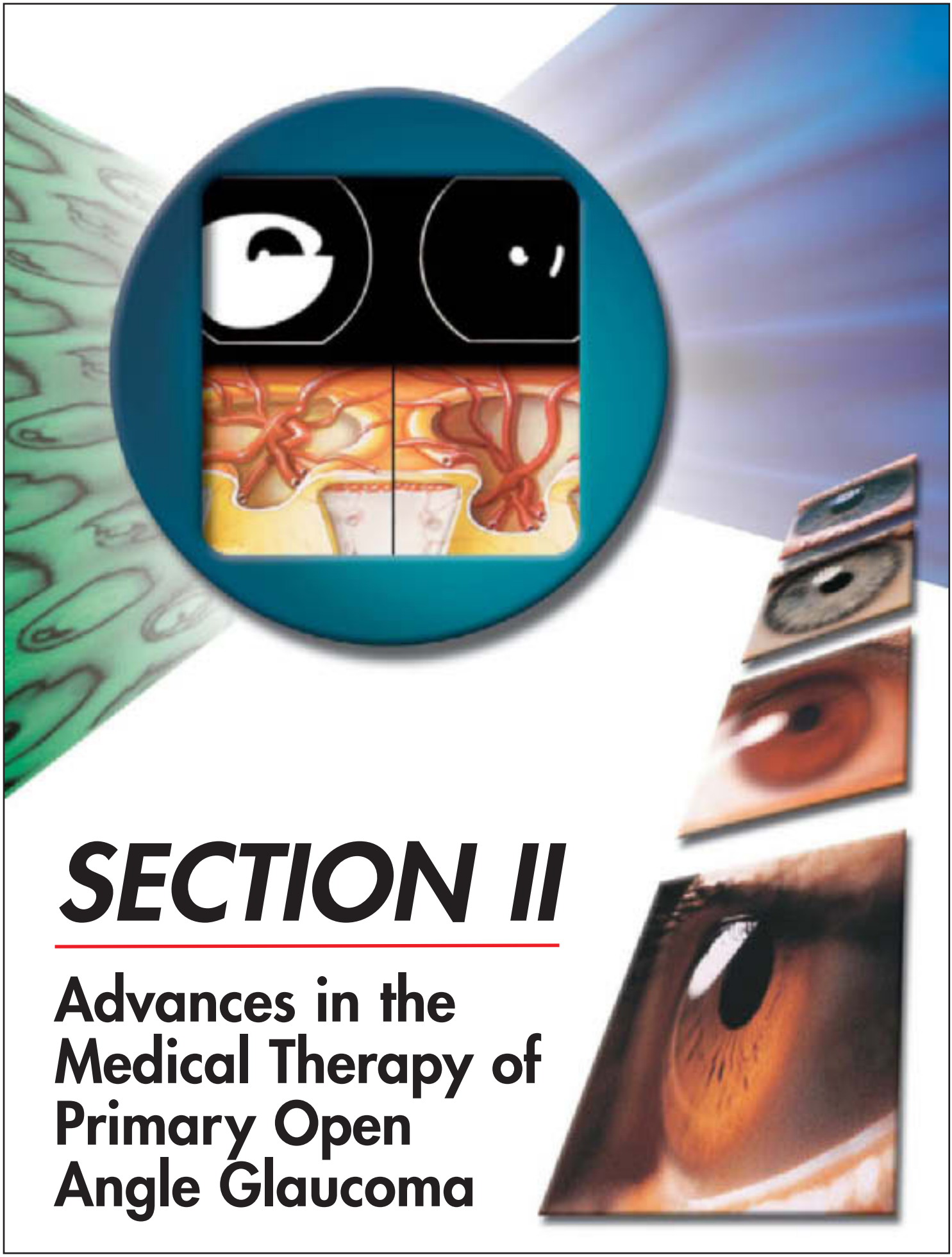
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SECTION II

Advances in the Medical Therapy of Primary Open Angle Glaucoma

Chapter 8
UPDATE ON MEDICAL THERAPY FOR GLAUCOMA

L. Jay Katz M.D., F.A.C.S.

An extraordinary number of new glaucoma medications recently have been introduced. Ophthalmologists have welcomed this increasing diversity of choices for their patients. At the same time, however, the choice between monotherapy and especially combination drug therapy has become confusing. The decision is based on a number of factors: efficacy, safety, theoretical benefits, and availability. A thorough understanding of the relative benefits of the current glaucoma medications may help guide practitioners in formulating their treatment regimen. Individualization of medical care will be shaped by the merits of the drugs, the patient's medical history and examination, and the patient's input.

BASIC PRINCIPLES

One-eye Therapeutic Trial

When starting a new topical glaucoma medication it is important to recognize that 1) patients may be "nonresponders" to certain drugs and 2) the diurnal intraocular pressure fluctuation may be wide. The ideal way of taking these factors into account is to perform a one-eye therapeutic trial, with the contralateral eye serving as a control. There may be a small crossover effect, especially with topical beta blockers, where the contralateral eye is affected by the drug instilled in the ipsilateral eye, but typically it is only a matter of 1-2 mmHg.

Nasolacrimal Duct Occlusion

A topical drug administered in the eye drains through the nasolacrimal duct towards the nasal mucosa, where it is absorbed into the systemic circulation. Appreciable serum levels are associated with certain topical drugs. Topically administering eye drops is akin to intravenously injecting a drug with target-tissue activity prior to first-pass deactivation through the hepatic portal circulation. In contrast, oral medications absorbed through the gastrointestinal tract are converted to a great extent to inactive metabolites by liver enzymes. With any topical drug, if the eyes are kept closed without blinking for at least 3 minutes, the tears are not pumped down the nasolacrimal duct. Combining eyelid closure with punctal occlusion by pinching the bridge of the nose up makes possible a two-thirds reduction in serum levels after topical drug administration.

Choosing a Glaucoma Drug

Individualization of care based on careful history-taking and examination is essential in recommending a glaucoma medication for a particular patient. Key factors include safety, cost, and theoretical advantages. Efficacy is measured by intraocular pressure reduction, which ultimately determines preservation of vision. Safety and tolerance concerns may be either ocular or systemic. Economic condi-

tions, either organizational (eg, health plans and formularies) or personal resources, will often dictate the availability of certain drugs. Interest abounds in non-IOP-mediated therapies such as medications that improve ocular hemodynamics or provide neuroprotection. Although promising, they have yet to be clinically validated. Therefore, the ideal glaucoma drug would be potent in lowering IOP, safe and well tolerated, available and affordable, and have other potential merit as a vasoactive or neuroprotective agent.

(**Editor's Note:** The Glaucoma Laser Trial with a 7 year follow-up concluded that for initial treatment of open angle glaucoma, laser therapy is as good and as safe as medical therapy. It is not as yet widely used as initial therapy because with laser therapy a successful result lasts on average 2 1/2 years and then regresses.)

"Target" Intraocular Pressure

Evidence-based medicine advocates have challenged the ophthalmology community to provide proof that lowering IOP changes the outcome of glaucoma. Meta-analysis has been used to tabulate data from various clinical studies. Table 1 shows an obvious trend indicating that eyes with lower IOP are less likely to have progressive visual field loss. In the Advanced Glaucoma Intervention Study (AGIS) patients who failed to be controlled on medical therapy were randomized to either argon laser trabeculoplasty or trabeculectomy as the next step.[1] When eyes were subgrouped according to the level of IOP it was clear that a lower IOP protected against visual loss as objectively graded with automated perimetry

Risk of visual field loss is related to IOP level

IOP (mm Hg)	% Field Loss	Relative Risk
<16	0.8	1
16-19	1.4	1.7
20-23	3.1	4.0
>24	8.4	10.5

Table 1.
This study shows a comparative indication that eyes with lower IOP are less likely to have progressive visual field loss.

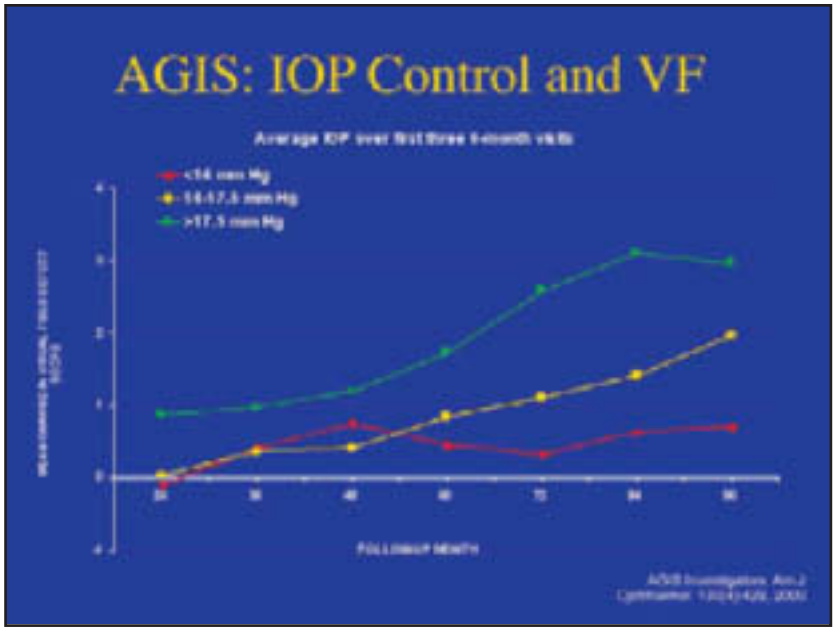


Figure 1.
Observe how eyes with IOP below 14 mm Hg fared better in the first 18 months than those with an IOP above 18 mmHg.

in the study (Fig 1). Eyes with an IOP consistently below 14 mmHg fared better in the first 18 months than those with an IOP greater then 18 mmHg. In a collaborative, prospective, randomized clinical trial patients with normal-tension glaucoma either were observed without treatment (controls) or were aggressively treated with medication, laser, or incisional surgery to lower IOP at least 30% below preoperative baseline levels.(2) Thirty-five percent of the control untreated eyes had visual field loss clearly due to glaucoma. In contrast, only 12% of the eyes in the treated group were judged to have deteriorated. Clearly the belief that an IOP below 21 mmHg is safe is no longer widely held. The guideline suggested by Chandler and Grant over 30 years ago that more severely damaged glaucomatous optic nerves require a lower IOP to stabilize the disease is now commonly accepted.

CATEGORIES OF CURRENT GLAUCOMA MEDICATIONS

Prostaglandin Analogues and Related Compounds

Latanoprost (Xalatan)

Ocular inflammation, uveitis, has been associated with hypotony mediated by prostaglandins, specifically the F2alpha subclass. A synthetic F2alpha analog, latanoprost is able to reduce IOP with minimal inflammatory effect. In a comparative trial, latanoprost used once a day in the evening was equivalent or slightly better in lowering IOP than

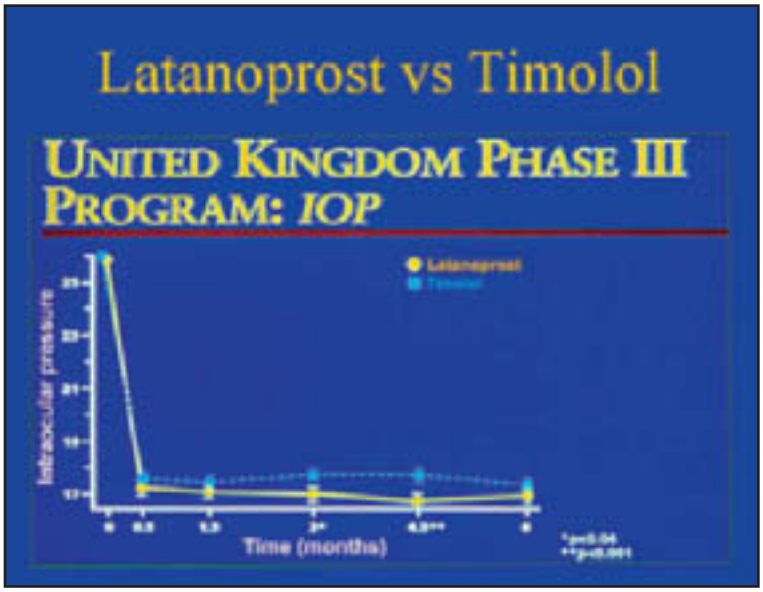


Figure 2.
Comparative trial of Latanoprost used once a day and Timolol solution used twice a day.

timolol solution used twice a day (Fig 2): the mean diurnal IOP reduction was 6.7 mmHg for latanoprost and 4.9 mm Hg for timolol.[3] Unlike timolol, latanoprost has minimal systemic side effects such as occasional flu-like symptoms, arthralgias, and headaches. These are rare and rapidly dissipate on discontinuation. Of more concern are potential ocular side effects. Irreversible iris hyperchromia presently remains only a cosmetic concern. Those with mixed irides (green and hazel) are most susceptible, with up to 60% changing after 2-3 years of latanoprost use. Stimulation of eyelash growth is commonly seen and poses no clinical problem, with rare exceptions of trichiasis. A more uncommon but serious side effect is the potentiation of uveitis-cystoid macular edema in high-risk patients: ie, those with pre-existing inflammation, diabetes, or retinal vein occlusions. Use of latanoprost perioperatively in intraocular surgery is controversial because of the risk of worsening inflammation and its relative lack of effectiveness in this setting. Reactivation of herpes simplex keratitis by topical latanoprost as seen with topical corticosteroid use has been reported in a clinical series and replicated in an experimental animal model. Latanoprost reduces IOP by enhancing outflow through the uveoscleral pathway, with no effect on the conventional trabecular pathway. Theoretically, this would make it ideal for combination therapy with drugs that are aqueous suppressants (beta blockers, alpha agonists, and carbonic anhydrase inhibitors).

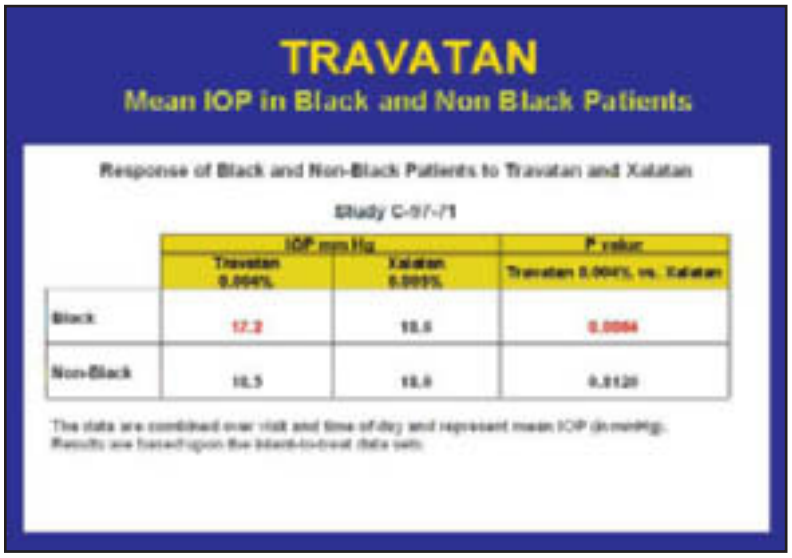


Table 2.
Comparative response of IOP measurements in blacks and non-blacks between Travatan and Xalatan.

Travaprost (Travatan)

Like latanoprost, travaprost is an F2alpha synthetic prostaglandin analogue. In binding assay studies it demonstrates a strong affinity for F2alpha receptors, perhaps even more than latanoprost. Compared with timolol, travaprost demonstrates a potency in lowering IOP similar to that seen with latanoprost. Travaprost has a response in the white population equivalent to that of latanoprost. However, travaprost appears to have a better response in African Americans. This difference was < 2 mmHg in mean IOP in a small sample size (< 50 subjects) in either arm, but this difference was statistically significant (Table 2). The side-effect profile of travaprost mimicks latanoprost, including iris hyperchromia and stimulation of eyelash growth.

Unoprostone (Rescula)

Available in Japan for several years, unoprostone has now been released in other countries. Although it is structurally similar to the prostaglandins, there may be clinically important differences. Prostaglandins are eicosanoids with a basic 20-carbon chain. Unoprostone is a 22-carbon molecule, classified as a docosanoid, derived from docosahexaenoic acid, a common substance in the retina. Unoprostone has a shorter duration of action then latanoprost, requiring twice-daily use for 24-hour coverage. It is less potent in IOP reduction then latanoprost or timolol in randomized clinical trials, with a typical mean IOP reduction of only 3-4 mmHg.[4] Of course, implicit when discussing mean IOP reduction is that there is standard devia-

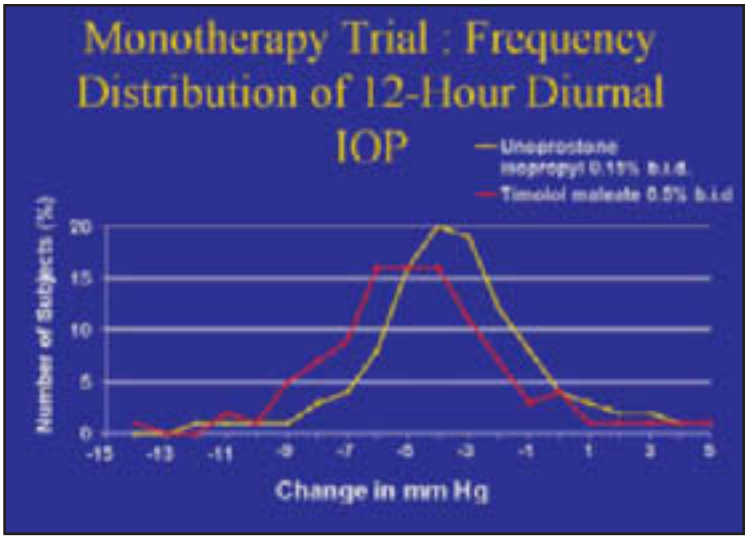


Figure 3.
Comparative monotherapy trial with frequency of distribution every 12 hours diurnal IOP between Unoprostone, Isopropyl and Timolol.

tion, with some subjects benefiting from a larger drop from unoprostone (Fig 3). Reported systemic side effects are rare, headaches being the most common. Ocular problems leading to discontinuation of unoprostone are predominantly related to surface toxicity with conjunctival injection and punctate keratopathy. Uveitis and iris hyperchromia have been reported but may be less frequent than with latanoprost. In animal models unoprostone has been demonstrated to be an endothelin-1 antagonist. Endothelin-1 is a potent stimulator of smooth-muscle contraction, which causes vasoconstriction when applied to blood vessels. Several studies have suggested that a defect in autoregulation of blood flow in some glaucomatous eyes may be the result of higher than normal levels of endothelin-1. Therefore, unoprostone may theoretically have a non-IOP benefit in eyes that have a prominent vascular role in the pathogenesis of glaucoma (eg, normal-tension glaucoma?). In this sense unoprostone may be neuroprotective. Preliminary evidence suggests that the mechanism of action of unoprostone may be an increase in the trabecular outflow pathway, which may also be mediated by its endothelin-1 antagonism. One study has reported a mild additivity of unoprostone to latanoprost in lowering IOP.

Bimatoprost (Lumigan)

In contradistinction to the prostaglandin analogs latanoprost and travaprost, bimatoprost is being categorized as a synthetic prostamide. Prostamides are derived from cell-membrane fatty acids in the anandamide pathway as opposed to the arachidonic pathway for prostaglandins. In support of this separate classification, bimatoprost in bioassay studies does not bind to any of the known prostaglandin receptors, including the F2alpha receptors. Unlike the other drugs in this category, bimatoprost is the active component and is not an ester-derivative prodrug that requires activation by esterase cleavage during corneal passage. As a once-daily drug, bimatoprost has been shown to be superior to timolol in lowering IOP. Data demonstrating the better efficacy of bimatoprost have been analyzed in a variety of ways: in terms of standard mean IOP reduction, effect on the diurnal IOP curve, ability to attain a set target IOP, and ability to reach arbitrary percentage IOP reductions below baseline. The mean IOP reduction at 3 months for bimatoprost (AGN 192024 – Editor) was 9.2 mmHg, compared

with 6.7 mm Hg for timolol (Fig 4).[5] Both timolol and bimatoprost maintain a consistent diurnal effect over 12 hours, although the magnitude of the IOP reduction consistently favors bimatoprost. The ability to reach a target pressure of 14 mm Hg was 30% for bimatoprost and 13% for timolol. The capacity to achieve a 30% IOP reduction below pretreatment baseline, as was the goal in the collaborative normal-tension glaucoma study, was possible in 63% of bimatoprost- treated eyes but in only 33% of those treated with timolol. A preliminary study suggests that bimatoprost is at least equivalent to latanoprost in potency and superior to it in achieving large IOP reductions such as a target of 14 mmHg (Fig 5). Despite the claim that it has a biological lineage different from that of the prostaglandin analogs, the side effects seen with bimatoprost appear to be identical to those associated with the prostaglandins. Hyperemia and pruritis may be more common than with latanoprost. These features appear most intense immediately upon starting bimatoprost. About 3% of patients enrolled in the pivotal studies discontinued bimatoprost because of these side effects. A dual mechanism of action has been reported, namely an increase in both uveoscleral and trabecular outflow pathways.

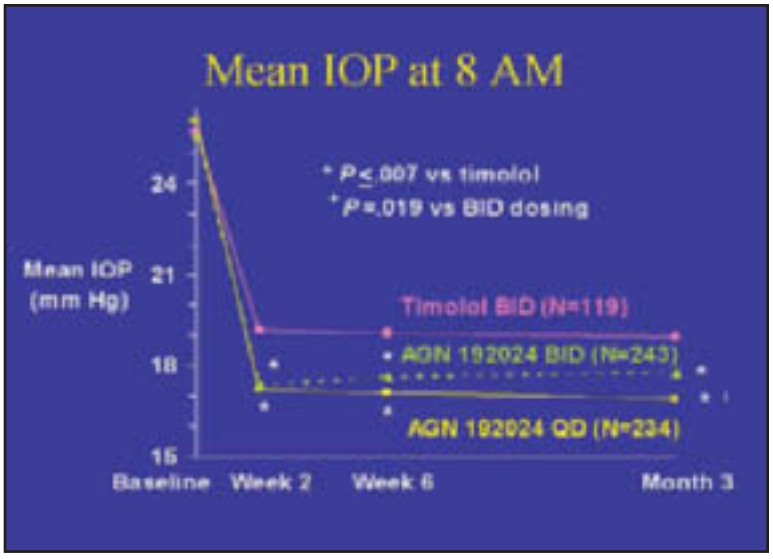


Figure 4.
Mean comparative IOP reduction between Bimatoprost and Timolol at three months of use.

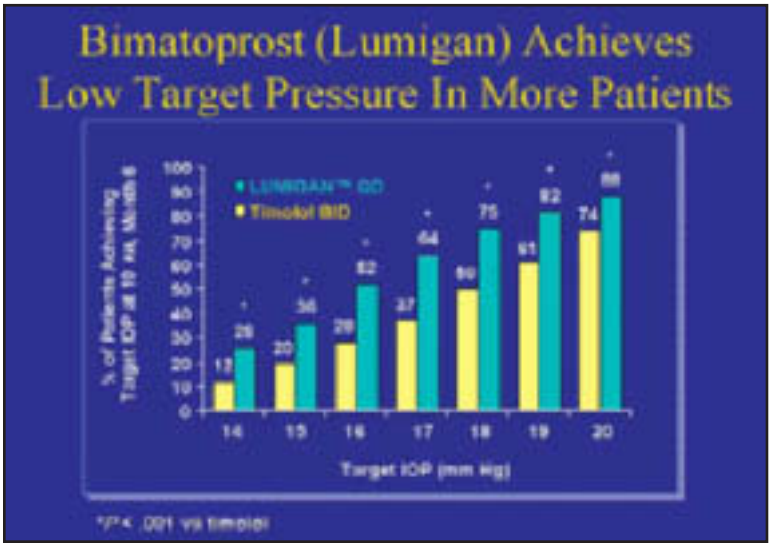


Figure 5.
This preliminary study demostrates how Bimatoprost works in comparison with Latanoprost in achieving large IOP reductions.

Beta Blockers Non-selective

Timolol Maleate (Timoptic)

For over 20 years since the introduction of timolol, topical beta blockers have been the most frequently prescribed class of glaucoma drug. They continue to be the "gold standard" that the Food and Drug Administration uses to evaluate all new glaucoma medications. Timolol solution has been demonstrated to lower IOP 6 mmHg on the average or 25% below baseline levels. Although there are "nonresponders," as seen with all glaucoma drugs, and tachyphylaxis, or long-term drift with loss of efficacy are well known, timolol has a long track record as an effective monotherapy and combination drug for the long- term treatment of glaucoma. Ocular tolerance has been excellent, with only occasional problems with surface irritation and dry-eye exacerbation. The greatest concern with topical beta-blockers is their potential for causing serious systemic side effects. Most familiar are the effects on cardiopulmonary diseases such as asthma and heart block. Underappreciated have been central nervous system problems such as depression, changes in mentation, and impotence. Ophthalmologists usually do not question patients to elicit such symptoms, and patients often do not appreciate or relate them to their eye drops. Use of the gel-forming solution Timoptic XE once daily has significantly lower serum levels as compared with the timolol solution, making it safer without sacrificing efficacy.(6) There is concern that some glaucoma patients, especially those with normal-tension glaucoma, are potentially harmed by nocturnal systemic hypotension. In the early morning hours if the blood pressure drops too low there may be a reduction in ocular perfusion and relative ischemia, with a susceptibility to optic nerve injury at "low" intraocular pressures. Since beta-blockers lower IOP by aqueous suppression and have little effect on aqueous production when patients are asleep, it is preferable to use a topical blocker only once a day first thing in the morning upon awakening. On this schedule the concern about beta-blocker-induced hypoperfusion to the optic nerve is minimized. Levobunolol (Betagan), timolol hemihydrate (Betimol), carteolol (Ocupress), and all the generic beta-blockers share a profile similar to that of timolol (Timoptic). If patients are on an oral beta-blocker, the response to a topical blocker may be blunted. In one study the IOP of patients not on an oral beta-blocker dropped the typical 6 mmHg when timolol drops were begun. On the other hand when patients were on a systemic beta-blocker, the IOP dropped on the average only 4.3 mmHg.

Relatively Selective Beta-1 Blocker

Betaxolol (Betoptic)

Betaxolol preferentially blocks beta-1 receptors (heart) 250:1 over beta-2 receptors (lungs). Therefore it is safer to use if there is a minor concern about potential pulmonary effects. Nevertheless, it should be used with a great deal of caution in moderate to high pulmonary risk cases since it is not exclusively a beta-1 blocker. Betaxolol has been noted to be less likely to affect the heart and central nervous system than timolol. This is at least partially explained by the fact that betaxolol is not as potent a beta-blocker. This clearly has been demonstrated in

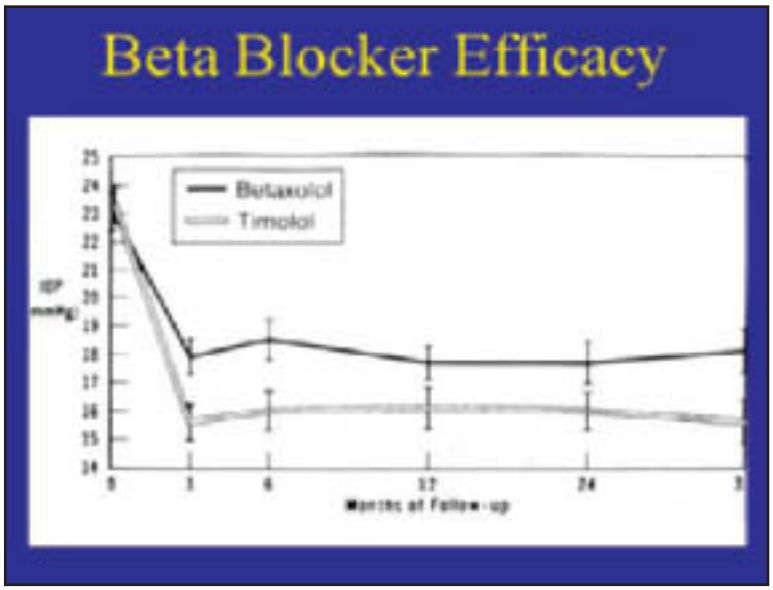


Figure 6.
Comparative study of a beta-blocker (Timolol) efficacy vs Betaxolol.

studies comparing the efficacy of a nonselective beta-blocker with betaxolol (Fig 6). Betaxolol-induced vasodilation of ocular vessels suggested in clinical studies and possible neuroprotective effects shown in experimental laboratory work have been attributed to a calcium-channel-blocker effect rather than to its beta-blocker function. The perimetry studies reporting better sensitivity scores in patients using betaxolol compared to timolol need to be confirmed with longer-term studies and larger sample sizes.

Adrenergic Agonists

Brimonidine (Alphagan)

The development of brimonidine represents the evolution of adrenergic compound modulation to yield a more effective and better-tolerated drug. Epinephrine and apraclonidine have a very high rate of allergy and only marginal long-term efficacy. Brimonidine is a highly selective alpha-2 agonist

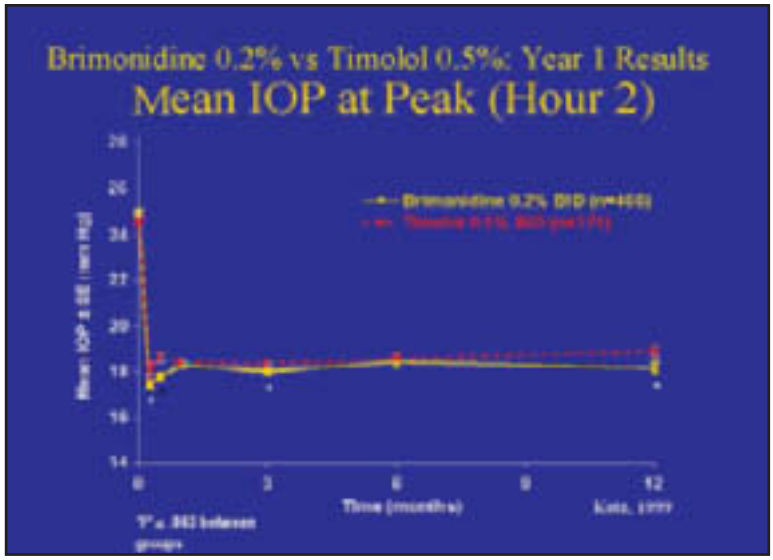


Figure 7.
One year follow-up of Brimonidine vs Timolol 0.5% in lowering IOP.

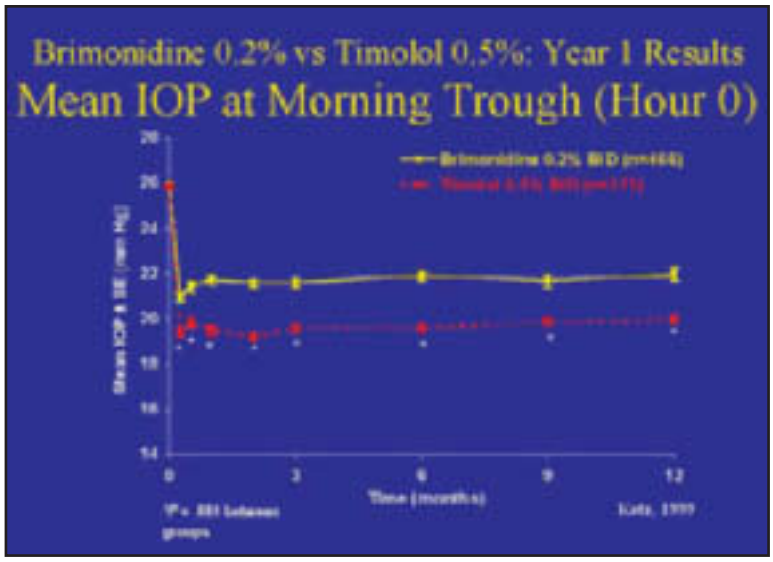
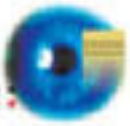


Figure 8.
Observe how at one year follow-up Timolol is clearly superior at the trough measurements.

(1800:1 over alpha-1 agonism). The alpha-2 effect appears to be the key not only for IOP reduction but also for the neuroprotection that has been demonstrated in animal studies with brimonidine. Undesirable effects such as vasoconstriction, eyelid retraction, and pupillary dilation are alpha-1-mediated events. Efficacy studies comparing brimonidine twice daily with timolol must be reviewed in terms of the peak (2 hours after dosing) and trough (12 hours after dosing and due for next dose) data. After one-year follow-up brimonidine was slightly more effective in lowering the IOP at peak measurements (Fig 7).[7] Timolol was clearly superior at the trough measurements (Fig 8). However, in follow-up data at 4 years for some of these patients the trough difference between timolol and brimonidine had disappeared. Whether tid dosing would provide better trough IOP control than the usual bid regimen remains unclear. Systemic side effects of brimonidine include lethargy and dry mouth, which, although common, only occasionally lead to discontinuation of the drug (< 3%). It is strongly advised not to use brimonidine in neonates and children because of the risk of profound systemic hypotension



and apnea, side effects also seen with timolol. In small children, with small blood volumes, drugs reach much higher serum levels than in adults. By far the most common reason for stopping brimonidine is the development of an allergic or toxic blepharoconjunctivitis in 10-15% of patients, with the onset usually after 3-4 months of therapy. In an effort to reduce the allergy rate brimonidine has been reformulated in a lower concentration (0.15% vs. 0.2%) and the preservative changed from benzylchronium chloride to Purite. The allergy rate in the initial trial decreased by more than 40%. The mechanism of IOP reduction has been attributed to aqueous suppression and improving uveoscleral outflow. Brimonidine has received the most attention in animal neuroprotection studies: optic nerve crush, ocular ischemia-reperfusion, phototoxicity, ocular hypertension, and neuronal culture models. Human trials are underway to attempt to clinically validate its neuroprotective capabilities.

Apraclonidine (Iopidine)

The first alpha agonist clinically used, apraclonidine proved very effective short term in blunting IOP spikes following laser and surgical procedures. However, long-term use has been hampered by tachyphylaxis of up to 30% and a 40% allergy rate.

Epinephrine (Epifrin, Glaucon, and Propine)

These adrenergic agents are both alpha- and beta-receptor agonists. Due to an allergy rate of 25-50% combined with a modest IOP lowering effect these agents are now rarely used.

Topical Carbonic Anhydrase Inhibitors

Dorzolamide (Trusopt)

Systemic oral carbonic anhydrase inhibitors (CAIs) are very effective in lowering IOP, but the extensive number of serious, debilitating systemic side effects associated with them make them a poor choice for long-term therapy in many patients. The introduction of topical CAIs was a welcome development and allowed wider application of CAIs with better tolerance, but they may not approach the potency of the systemic CAIs in certain patients. Dorzolamide as monotherapy requires tid dosing to provide 24-hour coverage. The extent of IOP reduction is approximately 5 mmHg, similar to that of betaxolol.[8] Although dorzolamide is far safer than oral CAIs, a number of systemic reactions have been reported, including a bitter, metallic taste, which is common, and there have been rare case reports of renal calculi and thrombocytopenia. Topical reactions to dorzolamide include transient burning, punctate keratitis, and allergic blepharoconjunctivitis. Carbonic anhydrase has an important physiological role in the corneal endothelium. There is continuing controversy as to whether patients with a compromised corneal endothelium (eg, corneal grafts, Fuchs' dystrophy) may be decompensated with the use of topical CAIs. In research involving ocular hemodynamic assessment patients treated with dorzolamide have demonstrated definite improvement in ocular perfusion. This has been postulated to be due to an increase in tissue CO2 levels, which is a known vasodilator. This added benefit of dorzolamide in glaucoma treatment remains unclear but intriguing.

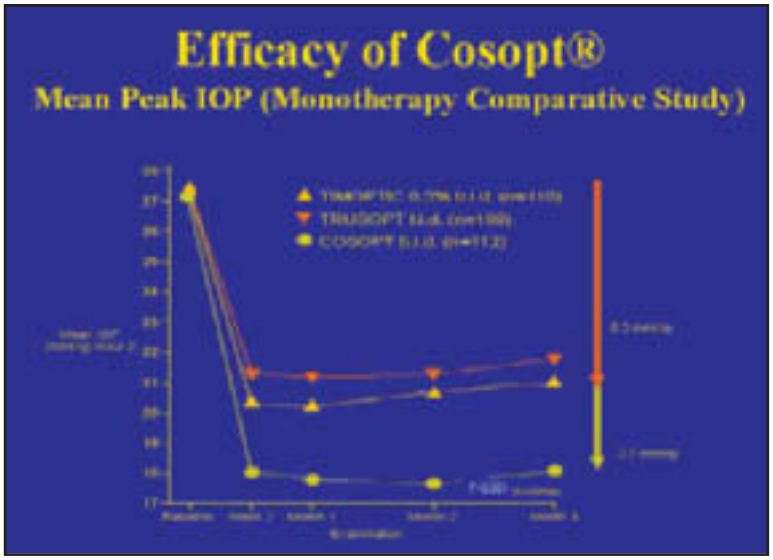


Figure 9.
Advantages and efficacy of Cosopt having two medications in one bottle.

Brinzolamide (Azopt)

Another topical CAI, brinzolamide, displays the identical efficacy in reducing IOP as dorzolamide with a tid schedule. The only differentiating feature is the lack of burning on administration, but since it is a suspension, some patients experience transient blurring of their vision.

Combination Medical Therapy

Fixed combination of Timolol and Dorzolamide (Cosopt)

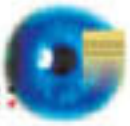
Having two widely used glaucoma medications in one bottle has a number of advantages: additive IOP lowering, improved compliance, and lack of the washout effect seen with consecutive eye-drop placement. Cosopt reduces IOP a mean of 9 mmHg at peak 2 hours after dosing, compared with a reduction of 6.3 mmHg with timolol alone and 5.4 mmHg with dorzolamide alone (Fig. 9).[9] In other trials an additional 2 mmHg reduction of eye pressure was observed in patients switched from timolol and dorzolamide to Cosopt.

Maximum Medical Therapy

In general, two to three bottles of glaucoma medication are encouraged before moving on to either laser trabeculoplasty or filtering surgery. The most attractive combinations involve prostaglandin-like drugs, beta blockers, brimonidine, and topical CAIs in various combinations.[10] When a further reduction in IOP is necessary, more emphasis has been placed on switching drugs than on simply adding or stockpiling them.. Replacement studies with latanoprost and brimonidine have confirmed the clinical utility of this approach. Miotics are still used as adjunctive therapy, especially in pseudophakic eyes, although availability has become an issue for some (Pilo-Ocusert, phospholine iodide).

CONCLUSION

Major improvements have been made in our ability to deliver more effective and safer drug therapy for glaucoma. A better understanding of the pathophysiology of glaucoma has provided better guidelines, with clearer outcome measures such as target IOPs and percent IOP reduction below baseline. In addition, the future holds great promise for therapies directed at improving ocular perfusion and neuroprotection, which may also help preserve the vision of our glaucoma patients.



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Chapter 9
MEDICAL MANAGEMENT OF PATIENTS WITH GLAUCOMA

Alan Robin, M.D.

New Developments in Diagnosing and Treating Glaucoma

In considering therapy for glaucoma, the ophthalmologist must consider both risks and benefits. The potential benefits must outweigh the risks before therapy is initiated. In my 20 years of pharmaceutical research, I learned to cautiously consider ocular side effects of systemic medications. The first consideration in developing treatment algorithms should be the welfare of the individual patient.

Several current studies are now testing traditional algorithms for treatment of glaucoma. The Glaucoma Laser Trial has been completed, with a 7-year follow-up. It has shown that for initial treatment, laser therapy is perhaps as good as medical therapy. Early results from the Advanced Glaucoma Intervention Study (AGIS) suggest that there are some racial differences that influence the effects of different algorithms of therapy. At least in whites, lowering the intraocular pressure (IOP) does make a difference. The Low Tension Glaucoma Study original results have corroborated this finding that lowering the IOP makes a difference in the patient's course of disease. These studies are yielding exciting new information that should enhance our knowledge about best treatment practices for glaucoma.

Another exciting development is that the number of possible medications for treating glaucoma has multiplied in recent years. In the past generation Pilocarpine and Diamox were the most advanced medications available. Since that time, the development of even more new drugs (such as Timolol) with particular benefits and applications has been exciting to watch. Ophthalmologists and researchers strive to develop new ways they can help their patients with glaucoma.

Nerve fiber layer analysis has become available as a diagnostic tool in the past few years. Improved perimetry has resulted in new algorithms, and it is now possible to do blue and yellow perimetry. These techniques make it possible to catch signs of glaucoma earlier, but assessment still involves looking at the whole patient rather than at specific indicators. There is no cookbook approach or algorithm that can be followed safely for all patients.

Identifying Risk Factors in the Patient

When beginning to consider therapy for glaucoma, it is advisable that the ophthalmologist should first look at these risk factors. Starting with the Baltimore Eye Survey, ophthalmologists have developed an understanding of the risk factors for glaucoma. The first risk factor to consider is eye pressure, although the risk of developing damage does not really occur until the pressure is over 30. We would absolutely treat a patient with a consistent pressure of 50 because of the high risk of developing visual field loss. Probably the pressure point at which

we would initiate treatment is 30 in patients who are young enough to go blind or develop visual disability within their lifetime.

The decision to treat must be made within the context of many other factors about the patient. For example, consider a 50-year-old patient with a normal visual field, a normal nerve fiber layer, and an optic nerve that is easy to evaluate with a 0.2 or 0.3 round symmetrical cup-to-disc ratio with no segmental loss and no retinal rim. If I am the patient and the risk of taking no medicine exceeded the risk of taking medicine, I certainly would want to be treated. The treatment for a patient with a moderately elevated pressure—for instance, 25—but who has a strong family history of blindness at a young age is also recommended.

It is also important to treat a patient with other risk factors such as pseudoexfoliation as soon as the IOP begins to increase. Coronary artery disease and systemic hypertension are other risk factors. According to the prevalence study, high myopia is not a significant risk factor, but we should watch patients with high myopia more carefully.

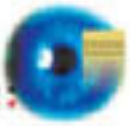
In other types of cases it would be preferable not to treat. We would not treat an 83-year-old patient with a pressure of 30, normal discs and fields, severe coronary artery disease, vascular occlusive disease to his neck, who had already had a severe stroke. This patient would probably die before he would become visually disabled from glaucoma.

Whether retinal vascular occlusion could develop from high pressure is a question still under investigation. There is good evidence that glaucoma or elevated IOP increases the risk of hemiretinal vein occlusions, central retinal vein occlusions, and branch vein occlusions. However, the converse has never been shown—that is, whether lowering the intraocular pressure would prevent a vein occlusion from occurring. We would routinely lower the pressure in the fellow eye of a patient who has a vein occlusion in one eye and a pressure of 25 or 26. No data, however, have shown that this treatment helps. Before there is visual field loss, earlier signs may indicate risk factors for or the presence of glaucoma. You should also looks for signs of afferent pupillary defect, disc asymmetry, cup asymmetry, and nerve fiber layer loss. It is more likely to treat patients with elevated IOP, with optic nerve drusen or optic nerves that have strange appearance. If the patient is a 5-year-old child with pressure of 25 or 26 and strange looking optic nerves, who cannot cooperate for a visual field, we prefer to talk to the parents and do not treat him/her until the patient is 10 or 11 and can collaborate to do a reliable visual field.

Another risk factor is optic disc hemorrhage. Although this can occur in patients who do not have glaucoma, usually a glaucomatous process is involved. The occurrence of an optic disc hemorrhage does not necessarily mean the patient's condition is worsening because repeat disc hemorrhages are very common, but it is an additional indication for treatment.

Let's take the example of a 60-year-old patient with a cup-to-disc ratio of 0.6 or 0.7 with pressures in the upper 20's and normal visual fields. The patient has no afferent defect and a nerve fiber layer that is difficult to analyze. You should evaluate the disc in this patient either at 6 month or yearly intervals. If there were no change in the disc, he would probably not get a visual field because it would be unlikely to have changed (this is a controversial viewpoint – **Editor**). If the patient's IOP went over 30, the patient developed an afferent pupillary defect, or the nerve fiber layer looked different, we would document the appearance of the optic nerve. If there were a change visible photographically, the patient would begin treatment. Otherwise we would continue to watch the patient.

For the patient with asymmetry of the optic nerves that is not congenital, 0.5 cup-to-disc ratio in one eye and a 0.7 cup-to-disc ratio in the other, we would expect an afferent pupil defect to exist even if there were no visual field defect and even if an optic nerve was difficult to evaluate. Until we saw the afferent defect, we would continue to follow the patient without initiating treatment.



Treatment for Glaucoma

Treatment Goals and Considerations

Especially after witnessing a considerable number of hazard treatments during the course of teaching residents, we believe it is very important to set a therapeutic goal before initiating treatment. The goal should depend upon the patient's age, life expectancy, and the degree of damage that has already developed. The Low Tension Glaucoma Study, for instance, set as a treatment goal a 30% decrease in IOP. If the patient already has split fixation in the central island, the ophthalmologist may want to treat more aggressively.

For ophthalmologists, the first goal is safety, because it is always important to do no harm. A treatment regimen should be individualized for each patient. This involves evaluating systemic issues such as the presence of asthma or coronary artery disease. The ophthalmologist must also keep in mind the eye color, and whether the patient is aphakic or pseudophakic.

You should start with a one-eye therapeutic trial because of the daily variation in pressure. One way of evaluating the efficacy of a medication is by comparing a treated eye to the fellow eye that is untreated. For example, if a patient has pressure of 30 in both eyes, the ophthalmologist could give him medication in just one eye. At the next visit if the pressure is 20 in both eyes, it can be inferred that the lowered pressure, which might have been attributed to the medication, was really due to diurnal fluctuation. Although this plan may necessitate an extra patient visit, all medications have risks, and we believed the added patient visit is warranted in order to ensure the effectiveness of the prescribed medication.

Another treatment goal should be to make the treatment regimen as simple as possible. Doctors tend to add and add to the patient's medications. Some experts discourage this tendency because compliance is critical in glaucoma therapy. A recent consideration has been whether or not neural protection should be an issue in how treatment is carried out.

The final issue, which is becoming much more important globally, is the cost of therapy. It may be misleading to look at the cost of therapy in terms of cost per bottle because different medications have different drop factors. For example, compare Timolol, which has a drop size of 32 microliters, to Levobunolol, which has a drop size of 50 to 60 microliters. Even if the bottles are priced comparably, Levobunolol could be 60% to 80% more expensive because the medications are used with the same frequency but Levobunolol yields fewer drops per bottle. A medication like Latanoprost, which came on the market 3 years ago, is very expensive but is used only once a day. Compared to medications such as Permoradine, which should be used twice or three times a day, it turns out to be cheaper per day.

Treatment Medications

Whereas many of these medications are relatively new, beta blockers have been available for more than 20 years, and there is more experience in dealing with them. When they are used in patients who do not have severe coronary artery disease, asthma, or chronic obstructive pulmonary disease (COPD), beta blockers are probably the best first-line therapy.

Our initial beta blocker of choice is Betaxolol because it is selective and seems to work better than nonselective beta blockers in avoiding exercise-induced tachycardia, changing lipid profiles, pulmonary constrictions, and central nervous system (CNS) effects. There is some question about whether Betaxolol is neural protective. Betaxolol is used twice a day; there is not yet much evidence to suggest that it can be effective when administered only once a day.

We believe the disadvantage of this drug is that there is a 2 mm mean difference in IOP in patients treated with Betaxolol compared with patients treated with nonselective beta blockers. It is not yet clear whether this mean difference results from a small difference in most people or because there is a particular group of patients who do not respond nearly as well to Betaxolol. When you consider issues like physician visits, diagnostic tests, and complications, Betaxolol can arguably be considered cost-effective. If Betaxolol does not work in an individual, it is important to try a nonselective beta blocker. Sometimes Betaxolol is usually not enough, which brings up the question of a second-line medication.

Some experts avoid using Timolol hemihydrate, Betimol, and Optipronolol since beta blockers usually have yellow or blue tops, the white tops of these drugs are confusing to both physicians and patients. In addition, Optipronolol has what we consider an unacceptably high rate of granulomatous uveitis associated with it.

If this regimen is not sufficient, the next choice may be Latanoprost. This drug is very safe and effective in the right individuals, although iris color changes can occur. Patients with light blue or hazel eyes should be told before they take the drug that this is a possible side effect.

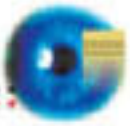
There have been reports on Rescula, another prostaglandin. Unlike Latanoprost, which is used once a day, this prostaglandin must be used twice a day. It is also somewhat less effective than Latanoprost and is associated with nausea. Some iris color changes have been reported even in a Japanese darkly pigmented population. The change in iris color, which seems to be caused by an increase in the number of pigment granules in pigment cells.

Although many physicians go to Alphagan or Brimonidine rather than Latanoprost because of the assumed neural protective effects of Brimonidine, we have experienced no convincing evidence that Brimonidine is neural protective. Brimonidine is a relatively highly selective alpha 2 antagonist. Some research on the alpha 2 type drugs like quinidine, apaquandine, and Brimonidine may have shown secondary neural protection of the optic nerve in rats, but several important questions need to be asked. We do not know whether the drug is safe enough to warrant the potential risk or whether there is a high enough concentration of Brimonidine when given topically as an eye drop instead of as an intraperitoneal injection in a rat to produce beneficial effects. A study reported by Joel Schuman in Archives of Ophthalmology in 1997 compared long-term Brimonidine treatment to long-term treatment with Timolol. In a 1 year study interval there was no difference in field loss between the two groups, and thereby no clinical evidence of neural protection.

I consider Brimonidine a third- or fourth-line drug for several reasons. It is one of the more expensive medications, and the side effect profile can cause problems. The alpha-2 stimulation decreases pressure but also increases sedation. Brimonidine is not as effective as Timolol maleate in lowering IOP, and Betaxolol is equally as effective as Brimonidine. There is a tight therapeutic index for Brimonidine in individuals who have problems with systemic hypotension; most ophthalmologists, don't measure blood pressure. Whereas it is easy to measure pulse rates to determine the appropriateness of prescribing a beta blocker, measuring blood pressure is logistically not easy.

Our next drug of choice is Cosopt, which is easy to work with. Questions have recently been raised about Cosopt. Cosopt is a combination of Timolol maleate and Dorzolamide. It is not as sensible a combination as a prostaglandin and a beta blocker now available in some countries. Cosopt is a combination in which both drugs work simultaneously to decrease flow. Cosopt also stings more than Timolol, and it is only 1 mm to 3 mm Hg more effective than Timolol alone.

If these drugs are not effective, you may try different combinations of a prostaglandin and a beta blocker. Sometimes we use a carbonic anhydrase



inhibitor, like Brinzolamide or Dorzolamide. If we find that one or two of these combinations are not effective, we go directly to ALT.

The combined use of Latanoprost and Timolol is already one of the more widely used treatments in the management of glaucoma in the U.S. With the release of "Xalacom" in Europe which consists of both drugs combined made available in one bottle the reduction of IOP has become more effective as well as simpler and comfortable for patients. This leads to better compliance.

Multicenter studies in the U.S. and Europe have demonstrated a statistically significant effectiveness of this combined medication ("Xalcom" in U.S. and "Xalacom" in Europe) over Timolol or Xalatan independently in reducing IOP and less side effects in one daily dose (every 24 hours). (**Editors** - Information obtained at the Glaucoma Meeting, May 24th, 2001, Spain). (**Editor's Note:** The latter medication is at present available only in some countries. Please consult your local representative). In the configuration under development by Pharmacia, one drug decreases flow and another increases outflow.

Argon Laser Trabeculoplasty (ALT)

Whether ALT is effective depends very much on the individual patient and the stage of glaucoma being treated. ALT does not work in people with traumatic glaucoma, uveitic glaucoma eye syndromes, and some forms of secondary glaucoma. In some people with diseases like pseudoexfoliation, the disease process continues despite ALT. Consequently, results are disappointing when the pressure returns to its pre-ALT level 2 years after the procedure.

In the right patient population, however, ALT is very good adjunctive therapy, but it should not be expected to be more effective than medication. Just as one medication cannot be expected to work in every patient, ALT cannot be expected to work in everyone. To realize that after 8 or 10 years ALT it is still effective in only 33% is not too bad considering the level of eye disease we are dealing with. If expectations are realistic, ALT can be understood as an effective procedure and a first- or second-line therapy. Hugh Beckman's glaucoma laser trial revealed that patients tolerated laser very well as the initial step. In terms of compliance and expense, ALT is probably superior. Clearly, for these reasons, it is much better therapy than medications for some types of patients.

We started doing ALT in 1978 after Jim Weiss discussed the procedure. At that time we thought that ALT would never work. But Weiss was right, and we took this occasion to apologize in public for his gloomy prediction about the procedure. ALT may even be a good first-line therapy for many individuals. Some choose not to have laser treatment, and ophthalmologists should try to be as unbiased as possible, because the answers about the best procedures to follow are still unclear.

The other approach that is becoming much more popular is the use of filtering surgery as a first-line therapy. The IOP can really be brought much lower—down to 10, 9, and 8— over a protracted time period through this technique. Filtering surgery works fairly well as a primary procedure. Perhaps we should worry less about the problems of cataract formation and endophthalmitis, as they happen acutely and make us aware of their presence, than about the patient who gives the impression of being compliant, yet is really not using his drops all the time. Over a 10-year period this patient will gradually lose visual field and optic nerve tissue. Operating initially might be doing this patient a favor. The answer to that question is still not clear; we are waiting for the results of more structured studies before we can answer that question definitively.

Chapter 10
THE ONGOING SEARCH FOR ETIOLOGY, PATHOLOGY AND MANAGEMENT

Balder P. Gloor, M.D.

THE SITE OF GLAUCOMA

Until the 17th century the site of Glaucoma was believed to be the pupil from antiquity. Until the 17th century the color of the pupil was used to differentiate four main groups of diseases of the eye: the black pupil stood for black star and amaurosis, the white pupil for Leukoma, the gray pupil for cataract and the green pupil for glaucoma or green star. Star derives from to stare. "Staraplint" or "staerblind" means a blind view (Mackenzie 1835 [45]).

Since the 17th century "Tension" or pressure became the criterion to differentiate between glaucoma "false cataract" and cataract.

Many scientists such as Beer[34] and others Mackenzie[45], contributed [1, 34, 48] but essential progress came with the invention of the ophthalmoscope by Helmholtz in the middle of the 19th century (1851) [33,55]. Von Graefe recognized immediately the significance of the excavation of the optic nerve head and he defined glaucoma as pressure, optic atrophy with excavation and field loss [29, 30]. So ingrained was the concept of glaucoma as the green cataract, the optic nerve had to be colored green as depicted by Jaeger in 1855 [35].

What Is Cause and What Is Effect?

Is Glaucoma primarily a disease of structures which can cause a rise of intraocular pressure (IOP) or a disease of the optic nerve head? v.Graefe [29.30] devoted a lot of thought to this question, which even today is an ongoing controversy lasting since 1855 until today!! **He voted for pressure!** But an excavated optic nerve head without any acute phase of increased IOP remained an enigma for him. Although v. Graefe with his iridectomy had invented a cure for pupillary block glaucoma, he understood neither the pathogenesis of this disease nor the mechanism of his operation, which is why he and many others used it without success - in POAG, which at that time was called chronic simple glaucoma[31].

What can we learn from this? There are surgical procedures which are effective although we don't understand what we do. This has not changed until today. Who for instance understands deep sclerectomy?

If IOP was essential, it had to be measured. The first tonometers like the one of Donders

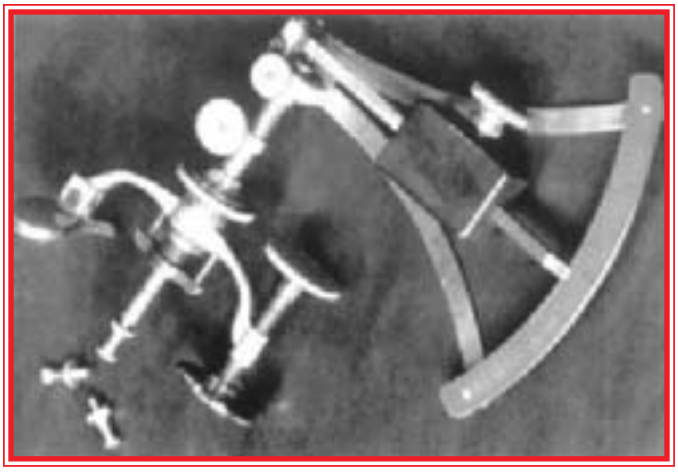


Fig. 1 The Tonometer of Donders (from Draeger [16]). The instrument could measure IOP only above 40mmHg!

(Fig. 1) [16] measured IOP above forty. This led to scientists talking about glaucomas with normal pressure, when IOP was high by our present standards and did not equate to our present concept of low tension glaucoma. Therefore it is inaccurate , although it is reported, to declare that true low tension glaucoma was known in the 19th century!

This illustrates that learning about glaucoma is dependent on the development of instruments for observation and measurement choosing the right scale and finding the right anatomical location.

Tonometry

Applanation tonometry standardized measurement of IOP. The Maklakoff Tonometer (Fig. 2a, b), introduced 1885 [16], was a simple and intelligent instrument. Russians have stayed with this

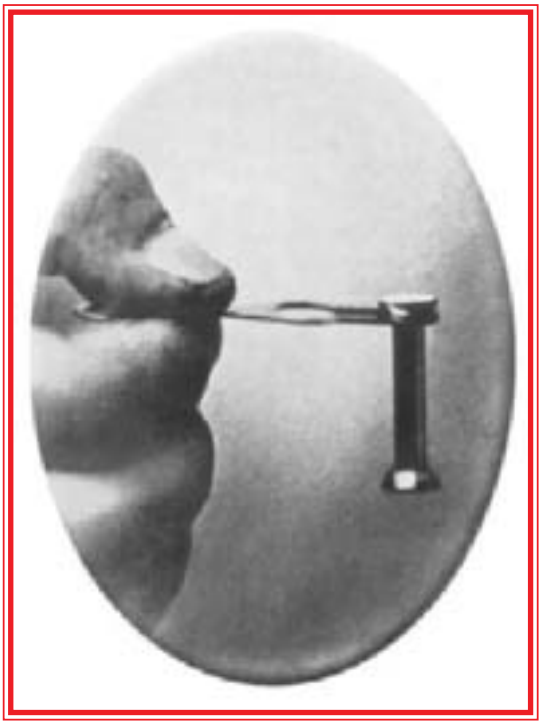


Fig. 2A

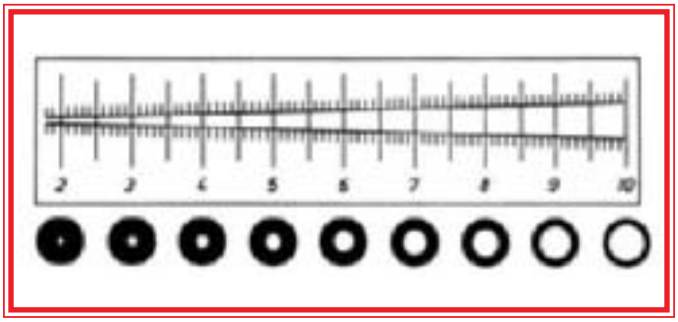


Fig. 2B

Fig. 2 A-B:

(a) (left) The Maklakoff Tonometer, an applanation tonometer introduced in 1885, served in Eastern Europe until recently (from Draeger [16]).

(b) (above) The surface of the tonometer was colored by black powder. After applanation of the cornea with a standarized pressure the diameter of the size of decolorized area (applanated area) was translated into the intraocular pressure.

but Central Europe and the USA turned to indentation tonometry using the tonometer invented by the Norwegian Schiötz. However, indentation tonometry has problems especially with scleral rigidity; which led to the creation of formulas like Friedenwalds [19] a useful byproduct was tonography and the insight it brought into outflow dynamics and resistance, summarized in the so called **Goldmann formula** [25]:

$$\text{Flow (ml . sec-1)} = \frac{P_{io} - P_v}{R} \quad \text{or} = (P_{io} - P_v)\, C$$

$$P_{io} = \text{Flow} \cdot R + P_v$$

P_{io} = IOP
P_v = Episcleral venous pressure
R = Resistance to outflow (tonography)
C = Facility outflow

The problem with Schiotz tonometry led Goldmann to develop his applanation tonometer in 1954 [26] which is still the standard of today.

Etiological Site

The etiological site of Glaucoma moved from **a disease of the ciliary body to the understanding of aqueous production and outflow through structures in the chamber angle** [20]. Essential contributions came from Leber, who worked on fluid exchange in the eye from 1873 until 1900 [41,42,43]. With his pupil Deutschmann [19] he realized that aqueous is formed by the ciliary processes, that it passes "Fontana's" space (the trabecular meshwork) and leaves the eye through Schlemm's canal (Fig. 3). This was challenged e.g. by Hamburger [32], in 1945 [17] Duke-Elder still discussed iris and/or ciliary body as sources of the aqueous. But in the years 1918, 1921 and 1923 Seidel delivered definite proof, that aqueous is formed by the ciliary body [56,57,58].

Gonioscopy

The modern classification of the glaucomas originated with gonioscopy by which means the site

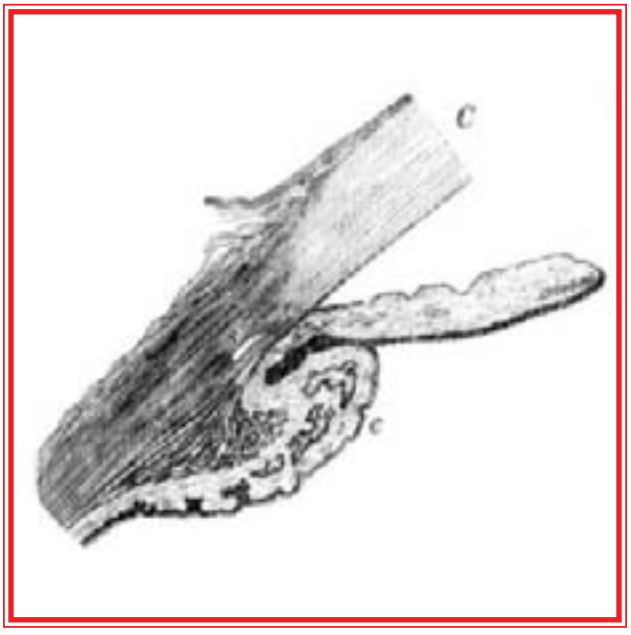


Fig. 3 One of Weber's histopathologic figures to demonstrate the obstruction of the outflow pathways as cause of acute glaucoma.



Fig. 4 Salzmanns comment to this picture in his article on "Ophthalmoscopy of the angle: "… 37 years old man, traumatic cataract. Incomplete circumscribed peripheral goniosynechia; pigmentation of the trabecular meshwork".

of different glaucomas could be localized. Salzmann could observe the angle with his lens and an ophthalmoscope (Fig. 4) [53,54], but with the Koeppe lens[38,39,40] (Fig. 5) the angle could be visualized with slit lamp-biomicroscopy. Vogt[49,64,65,66] after several disputes with Koeppe, wrote in a footnote: "Several years ago Koeppe developed instruments to bring the disc and macula within the reach

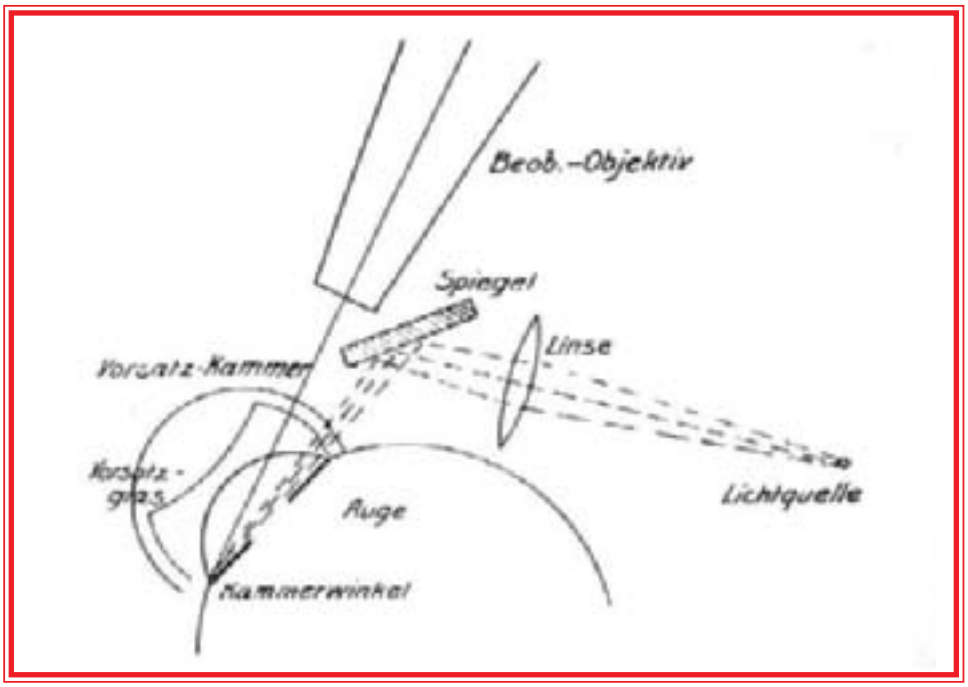
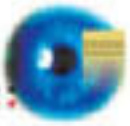


Fig. 5 Gonioscopy with the Koeppe lens gained wide acceptance in the United States of America, less in Europe. Rays of observation and rays of illumination are separated. Koeppe used for observation a binocular microscope from the beginning.



of slit lamp examination. This method is not taken into account, because it is without practical relevance. This is also the reason not to consider microscopy of the chamber angle and ultramicroscopy" (64).

This shows two things: First: Giants of Opthalmology can make gigantic mistakes; second: It is wise, not to say too much about the future.

Understanding Pathophysiology

Troncoso(63), Trantas(61,62), Barkan (3,4,5,6,7) and Busacca(12) also made contributions to gonioscopy. By gonioscopy the pathophysiology of most of the secondary and angle closure glaucomas became understood and could be separated from primary open angle glaucoma. **Primary open angle Glaucoma (POAG) remained and remains the challenge!**

POAG due to overproduction of aqueous humor or is it a disease of the outflow pathway? This was the question. Overproduction was clearly ruled out by Brubaker(10). Trabecular meshwork, Schlemms canal, and collector veins became the site of POAG.

The problem remained, that the resistance to outflow at the trabecular meshwork could not be fully explained mathematically or by morphology(46) nor by the changes in the trabecular meshwork in glaucoma patients, because these are not too much different from age dependent changes.

Low Tension Glaucoma

Population studies on the distribution of IOP values using accurate tonometry measurements uncovered a new problem. There was questionable correlation between IOP, optic nerve atrophy and visual field loss. A finding that questioned the role of raised IOP in the etiology of optic atrophy and visual field loss. (e. g. Klein 37, 9). These studies led to the concept of enumerating risk factors other than IOP for developing optic atrophy and moving, in some forms of Glaucoma, the site of the disease process into the site of damage, in so called low or normal tension glaucoma.

Goldmann would not accept this diagnosis unless the diurnal IOP curve was normal including measurements in the early morning in the supine position. **Sampaolesi**, who manages around 6000 glaucoma patients finds low pressure glaucoma in a small percentage only. 50% of the patients who were referred to our hospital for evaluation of low pressure glaucoma had another disease leading to pseudoglaucomatous optic atrophy! (47)

Goldmann stated: **" Under the term "Glaucoma" (green cataract) diseases are included, which are the consequence of increased intraocular pressure and of which the essential is this rise of intraocular pressure" (28).**

Goldmann's statement is a definition, and outlines the clinical parameters of glaucoma.

Glaucoma Optic Neuropathy

When IOP and increased outflow resistance was no longer considered by some to be the cause of glaucoma, then "Glaucoma is optic neuropathy" became the slogan and glaucoma became a basket full of etiological factors (Fig. 6). An entity formerly defined by damage from increased IOP is now relegated to a vast amount of more or less hypothetical causes of an optic atrophy with excavation, which is considered morphologically non-specific.



Fig. 6 Distribution of intraocular pressure and correlation to visual field loss in population studies left glaucoma as a basket full of risk factors!

Acceleration in Introduction of New Drugs

As for therapy, pressure lowering agents remain the heroes on the battle field: This is the moment to look into drug therapy over the last 125 years. From Pilocarpin to Adrenalin to Acetazolamide to the betablockers and the newest drugs of the last decades. The development and the introduction of new drugs into daily practice have taken on a logarithmic acceleration.

Table 1: NEW PRESSURE LOWERING GLAUCOMA DRUGS (a logarithmic evolution?)

		Δ years
Pilocarpine (Weber!)	1876	
		44
Adrenaline	1920	
		34
Azetazolamide (Diamox®)	1954	
		22
Dipivefrin	1976/8	
		4
b - Blockers	1980	
		2
Apraclonidine	1992	
		1
Brimonidine	1993/5	
Unoprostone (Rescula®)	1994	
Topical CA inhibitors	1995/7	
Latanoprost (Xalatan®)	1995	
Bimatoprost (Lumigan®)	2001	

The advent of the Beta-Blockers brought the large pharmaceutical firms into Ophthalmology. With Apoptosis came the move from mechanics to molecularbiology and molecular genetics. Neuroprotection appeared on the horizon. (See Chapters 11, 12, 13-**Editor**).

Neuroprotection

Looking at optic neuropathy and neuroprotection: **Where is the site of damage?** Leonard Levin's [44] research suggests that the site of damage are the axons at optic disc. (Chapter 11-**Editor**) The damage of the ganglion cells is secondary. Beginning and ongoing apoptosis is therefore not the primary target for a neuroprotective therapy. Two hypotheses on the cause of damage to axons have existed since glaucomatous excavation of the disc was recognized in the middle of the 19th century. The first is the **vascular hypothesis** - the second **pressure by its own**!

The available evidence suggests that all the neuroprotective agents[67], which are involved at the level of induction and progression of apoptosis of the body of the retinal ganglion cell are not the ideal neuroprotective agents, such as genes inducing or hindering apoptosis.

Editor's Note: For further valuable information on Neuroprotection, we refer you to the special group of Chapters on "Neuroprotection and Neuroregeneration". (Chapters 11, 12, 13-Editor).

Evaluating Therapy

Another major problem remains; how to measure therapy.

Before we try to answer this question we have to move once again back into history: Methods to measure damage had reached a certain level long before the pathophysiology of the rise of intraocular pressure was understood.

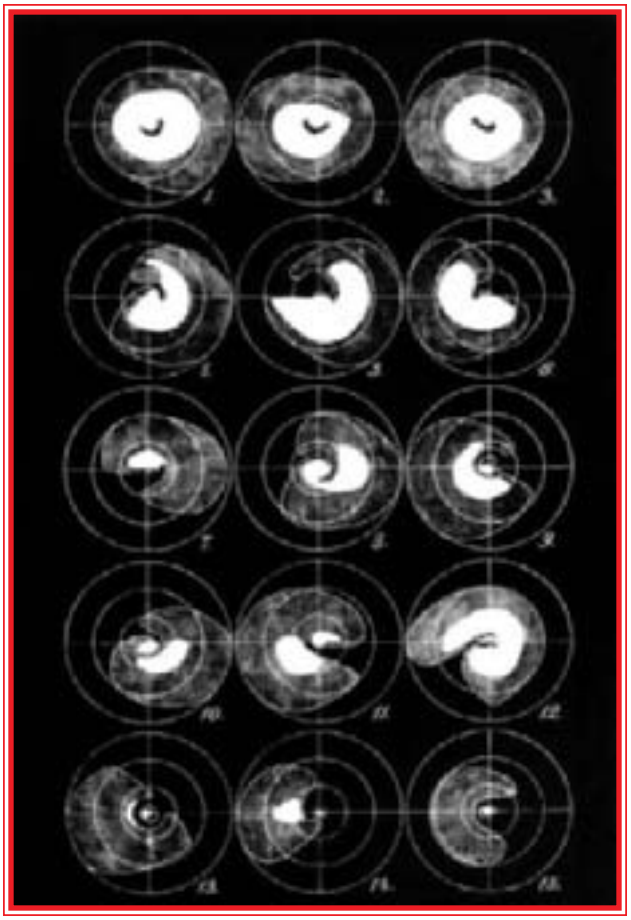


Fig. 7 Rönne presented 1909 a rich collection of drawings of glaucomatous field defects: Bjerrum scotomas, nerve fiber layer defects of any size, nasal steps.

Steps in **visual field testing** are connected with the names of Bjerrum[8] and his pupil Roenne 1909 [24,51,52]. They demonstrated the field loss in Glaucoma (Fig. 7). The improvements to the perimeter, which Goldmann presented in 1945, was the standardization of luminance of the background and

of the test objects [27]. But the earliest documentation of visual field loss with present day technology does not translate to earlier detection of glaucoma as shown in a modified scheme of Read and **George Spaeth**[50] (Fig.8). **With the earliest demonstration of field loss glaucoma is not diagnosed before the beginning of the end stage, although this end phase may last 10 or more years**.

Fluctuations of light sensitivity in perimetry as reported over many years of evaluating automated perimetry in 1983, 1985 and 1986 (Fig.9) [20,21,22,23] is the reason, why evaluation of progress or stabilization of field loss is so extremely difficult – and makes serious testing of glaucoma drugs, when this has to be more than just evaluation of the IOP lowering effect, a nightmare. This will be

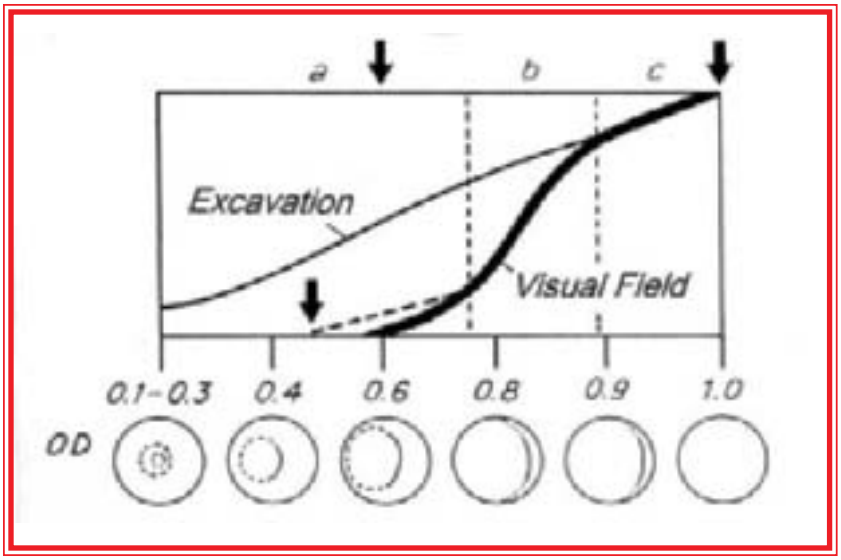


Fig. 8 As presented in the modified scheme of Read an Spaeth, automated perimetry could move earlier (optional!) detection in relation to cupping of the disc approximately only from a C/D ratio of 0.6 to a C/D ratio of 0.5 (arrow).

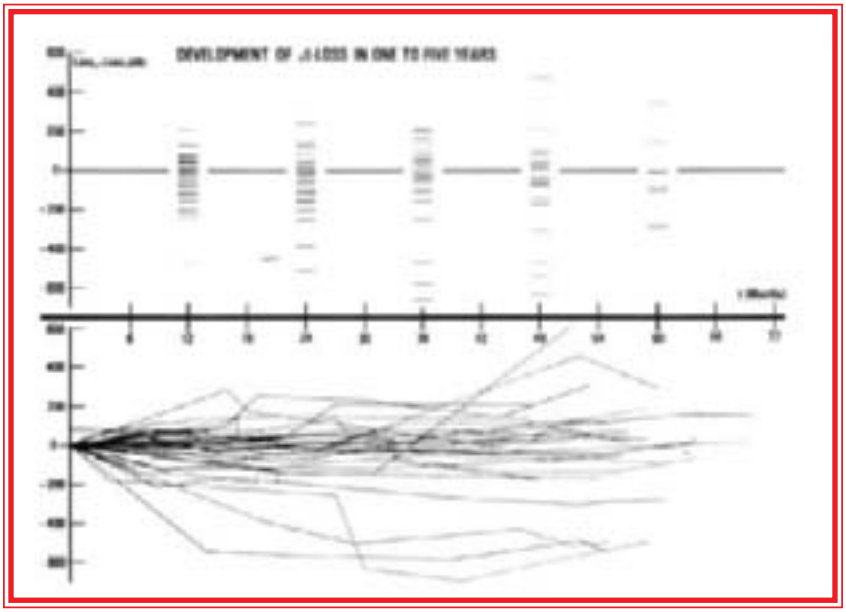
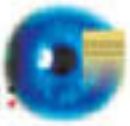


Fig. 9 Fluctuations of light sensitivity over 5 years: Development of „Total Loss", as defined by Bebié and Fankhauser, in program Delta Series for program 31 and 33 of the OCTOPUS over 1-5 years in 35 eyes with POAG. The value found at the first examination is zero. Curves with negative slope indicate gain, those with positive slope show additional loss. Be aware: At the beginning gain exceeded loss, by the end of the examination period gain and loss were about equal.



even more pronounced, as soon as neuroprotective drugs will come into clinical evaluation!!

The difficulties with field testing stimulated the development of other devices to recognize the damage earlier. This was and is papillometry.

Stereo-Planimetry can establish progress of the disease earlier than perimetry, as we reported in 1985[15,18,20] and – in clinical practice today earlier than with Laser Scanning Ophthalmoscopy or nerve fiber analysis, but it is very time consuming - . The most recent papers [11] do not clearly report, how many nerve fibers must be lost, before results are outside of the error of measurement. These are approximately at least **30,000 to 50,000 axons**!

We come back to the question: How to measure the effect of therapy? To capture the starting point of glaucoma is almost impossible. **Progression or not Progression** – this is the pertinent question! The undeniable standard to establish the influence of a given therapy on progression is the prospective double blind masked controlled clinical trial.

This standard is only reached for the IOP lowering effect of drugs and - very recently only -, lowered IOP correlated with function [13,59,60] but in no way for **Calcium channel blockers, Magnesium, Glutamate inhibitors, Gingko and any other neuroprotective drugs**.

When it comes to evaluate neuroprotection, the difficulties with drug therapy will become even more pronounced compared to pressure lowering drugs. It will be extremely difficult to convince ethical committees to test these drugs without combination of a pressure lowering substance. The measuring instruments we rely on are tonometry, morphometry and functional tests. The data bases of standard automated perimetry (SAP) and morphometry are large enough to allow the application of these instruments in large scale multicentre studies. In regard to more sophisticated methods such as short wavelength automated perimetry (SWAP) to catch small bistratified ganglion cells, frequency doubling automated perimetry (FDT), motion and flicker perimetry to evaluate magnocellular ganglion cells [36], the data bases are insufficient.

After an excursion into a mass of risk factors glaucoma research seems to return to the site of outflow resistance. Recently much research has focused on this site.

The move from IOP as the mediator of the cause of glaucoma to a disease of the optic nerve caused by a conglomeration of risk factors of which IOP is only one may be considered as a change of paradigm.

The competition between these two rivals is ongoing. But if in the definition of glaucoma IOP is left out, one should critically ask how much preservation of function has been achieved to this day from all the proposed treatments of all the other risk factors? When it comes to treatment, all speculations on risk factors come back to earth [2]: (See Editor's note below) at present the only proven glaucoma treatment consists in lowering the intraocular pressure, but as a second step and adjunct treatment neuroprotection seems to have a future.

(Editor's Note: Dr. Gloor makes a good point. However, the appreciation of risk factors for glaucoma does separate those individuals at greater **risk** of developing glaucoma. These individuals should be more aggressively monitored.)

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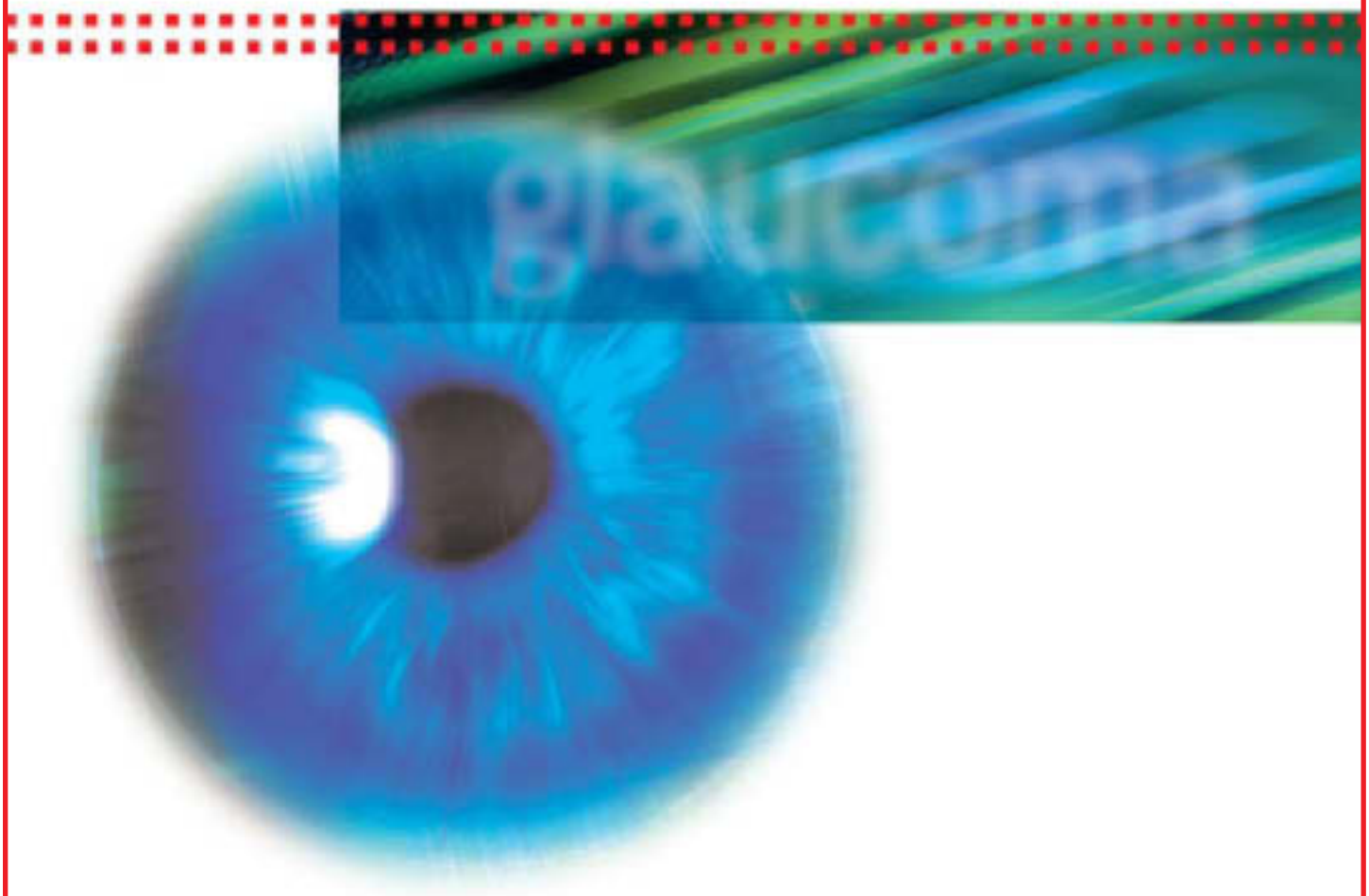
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NEUROPROTECTION and NEUROREGENERATION



Chapter 11
PRESENT STATUS OF NEUROPROTECTANT AND NEUROREGENERATIVE AGENTS IN GLAUCOMA

Leonard A. Levin, M.D., Ph.D.
Robert W. Nickells, Ph.D.
Paul L. Kaufman, M.D.

All glaucoma therapy is currently directed at lowering the intraocular pressure (IOP). IOP undoubtedly plays a causal role, albeit not necessarily an exclusive one, in many, if not most cases of glaucomatous visual loss. However, attacking or bypassing the trabecular meshwork, ciliary muscle, and ciliary processes, which are the target tissues for all our current treatments, completely neglects the retinal ganglion cells and their axons, the dysfunction of which is directly responsible for the visual loss. Only recently has knowledge of the mechanisms of neuronal death and its prevention, delay, or even reversal following a variety of insults reached the point where we can seriously entertain the possibility of glaucoma therapy directed at the retinal ganglion cells or their axons.

Neuroprotection

Death of retinal ganglion gells is the final common pathway of not only glaucomatous optic neuropathy, but all optic neuropathies. Although there is controversy about whether the primary insult occurs at the level of the axon or the cell body, the irreversible nature of the disease process reflects the loss of the retinal ganglion cell, probably via a suicide-like cell death process called apoptosis. Apoptosis is a type of programmed cell death that is actively used by cells during development and in tissue homeostasis. It is a cell-autonomous phenomenon, in that the death of the cell is already pre-programmed in its genes. When the cell receives the appropriate signal, it executes a program which induces it to commit suicide. This signal is neurotrophin deprivation during normal development, a process by which 50% of the ganglion cells are eliminated. Studies have recently demonstrated features consistent with apoptosis in experimental and clinical glaucoma, as well as other disorders in which the optic nerve is transected or becomes ischemic. The fact that retinal ganglion cells undergo apoptosis raises the tantalizing possibility that glaucoma may be a disease in which retinal ganglion cells accidentally receive an ill-timed "developmental" signal to begin apoptosis.

Although a wide variety of hypotheses explaining glaucomatous optic neuropathy have been tendered, including blockage of retrograde axonal transport, ischemia to the peripapillary nerve head, alterations of laminar glial or connective tissue, direct effect of pressure on retinal ganglion cells, and most recently, excitotoxic death mediated by a specific type of receptor for the neurotransmitter glutamate, in all of these mechanisms death of retinal ganglion cells is the end result. While most attention has been focused on understanding the pathophysiological mechanisms of glaucoma primarily with respect to pressure, it has become clear that protec-

tion of the retinal ganglion cells (neuroprotection) is an alternative way of preventing the progression of glaucoma, no matter what the mechanism.

A broad range of pharmacological interventions are therefore candidates for preventing retinal ganglion cell death in glaucomatous optic neuropathy. While most are only studied in animal or tissue culture models, some have been used in humans for other neurodegenerative disorders. These include preventing the initiation of the apoptosis program, protection of undamaged but at risk axons and ganglion cells from noxious stimuli released by proximate damaged tissue or retrograde axonal degeneration, and rescue of marginally damaged axons and ganglion cells (Table 1). Depending on the agent, the route of delivery could be intravitreally, transscleral, topical, oral, intravenous, via a viral vector, or via immunization.

Neuroregeneration

Attempts to regenerate ganglion cell axons presuppose a living ganglion cell. Understanding the mechanisms by which ganglion cells die may suggest mechanisms for saving them. However, once interventions become available to stabilize, or even reverse, retinal ganglion cell loss in glaucoma, then regeneration of the injured or absent axon will become necessary.

Goldfish and other lower animals differ greatly from humans and other mammals with respect to retinal ganglion cell death as a result of axonal damage. For example, goldfish retinal ganglion cells are able to re-extend their axons and establish connections with the brain. Understanding how simple animals are able to regenerate their nerves may eventually allow us to apply molecular

TABLE 1

Strategies for Preventing Retinal Ganglion Cell Death

Prevention of Initiation of the Apoptosis Program

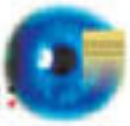
- Brain-derived neurotrophic factor (provides neurotrophin delivery to the retinal ganglion cell)
- Forskolin (increases level of cyclic AMP)
- Signal transduction inducers (to mimic the effect of binding of the neurotrophin)

Protection of undamaged but at risk axons and ganglion cells from noxious stimuli released by proximate damaged tissue or retrograde axonal degeneration.

- Antagonists to NMDA glutamate receptor subtypes (block excitotoxicity)
- Ca++ channel blockers (block the effect of excitotoxicity)
- Anti-oxidants/reactive oxygen species scavengers (block the program by which apoptosis is signaled)
- Active or passive immunization against myelin basic protein (MBP)

Rescue of marginally damaged axons and ganglion cells

- Anti-oxidants/reactive oxygen species scavengers (decrease levels of toxic oxygen radicals)
- Nitric oxide (NO) synthase inhibitors (block formation of highly reactive peroxynitrite from NO and superoxide)
- Lazaroids (block lipid peroxidation)
- Up-regulation or delivery of anti-death genes (bcl-2, bcl-xL), possibly via viral vectors)
- Active or passive immunization against myelin basic protein



and cellular techniques to induce regeneration of mammalian central nervous axons, which would be an important step in therapy for glaucomatous optic neuropathy. Alternatively, a better understanding of why peripheral nervous system axons can regenerate, when central axons do not, might similarly help in neuroregenerative strategies. It is known that retinal ganglion cells regenerate axons into peripheral nervous system grafts (e.g. sciatic nerve) apposed to a cut optic nerve, but not into CNS tissue. The non-permissive nature of the optic nerve substrate for axonal elongation is researched intensively, and likely is in part due to myelin components or their by-products.

Recently, it has become likely that the nature of the immune response (or lack thereof) at the site of injury may be responsible for reduced clearance of inhibitory molecules, resulting in blockade of regenerating axons. For example, while resident optic nerve macrophages (microglia) may increase in density at an optic nerve lesion, they may be impotent with respect to their ability to phagocytose degraded myelin. Thus, the inhibitory myelin components that remain may prevent axonal regeneration. Finally, it is possible that a peripheral nervous system graft actively supports regeneration by releasing a diffusable factor.

Collectively, these findings raise the exciting possibility that surgical and immunological manipulations presently done in animals may eventually be realized in patients with glaucoma. Even more exciting would be the development of pharmacological agents which would directly or indirectly affect the regulation of retinal ganglion cell axonal extensions via the immunological and/or biochemical mechanisms described. Some possibilities are listed in Table 2.

At present, no therapy other than reducing IOP has been proven to slow the progression of glaucomatous optic neuropathy. However, two drugs, memantine (a glutamate receptor antagonist) and brimonidine (an a2-adrenergic agonist), which have

TABLE 2

Strategies for Regeneration of Retinal Ganglion Cell Axons

Utilize the ability of axons to extend into peripheral nerve grafts

Autologous sciatic nerve or other nerve grafts
Donor grafts with appropriate HLA matching (if needed)
Use purified or engineered molecules from peripheral nerve to induce extension
Pharmacologically or genetically induce peripheral nerve molecules in optic nerve

Regulate the immune response within the optic nerve

Autologous activated macrophages to phagocytose myelin debris
Induce recruitment and activation of macrophages in situ
Induce activation of astrocytes and/or other non-constitutive phagocytic cells
Active or passive immunization against myelin basic protein

been effective in animal models of ocular hypertension or other types of optic nerve injury, are currently in human clinical trials. The intense research activity being devoted to the study of optic neuroprotection holds great promise that in the foreseeable future we will have glaucoma therapies directed specifically at protection, rescue or regeneration of the optic nerve.

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Chapter 12
MECHANISMS OF OPTIC NERVE INJURY IN GLAUCOMA

Robert L. Stamper, M.D.

Current Concept of Glaucoma

A progressive optic neuropathy characterized by specific morphological changes (optic disk cupping) resulting in loss of retinal ganglion cells (RGCs) and RGC axons. The RGCs die by apoptosis (cell suicide). This process is also characterized by visual field loss and other functional changes e.g. perception of color, contrast sensitivity and , movement.

Ganglion Cell Death and Apoptosis

Balance Between Injury and Survival

The fate of the RGC is a balance between Injury and Survival and between cell death and cell survival signals. Ganglion cells die in glaucoma from a form of programmed cell death called apoptosis. Apoptosis is a less dramatic form of cell death than necrosis and allows cells to die in a controlled, non-inflammatory fashion; this process is necessary for normal renewal of tissues such as corneal epithelium and skin. (In neural tissues, however, the loss is of permanent character – **Editor**) (Figs. 1 A-B).

Systemically, apoptosis is triggered by a variety of chronic processes including radiation, chemical injury, chronic ischemia, and chronic mechanical injury. In glaucoma, ganglion cell injury and eventual death may be caused by several factors including mechanical stress, blockage of axoplasmic transport, chronic ischemia, metabolic toxins, genetic influences and immune phenomena.

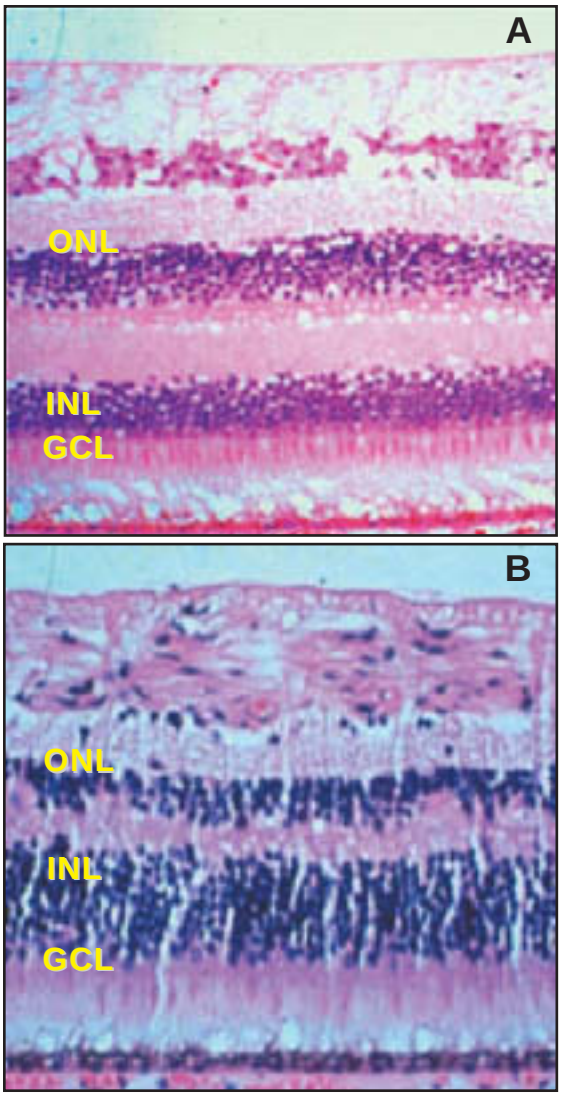


Fig. 1 A-B: Loss of Retinal Ganglion Cells.

Histological comparative changes between ganglion cells layer (GCL), internal neural layer (INL) and outer neural layer (ONL) of normal cells (1-A) and dead cells (apoptosis) (1-B). This reaction is mediated by a variety of processes that allows cells to die.

Activation of Apoptosis Process

The Role of Kinking of Ganglion Cell Axons

Glaucoma causes collapse of the lamina cribosa plates which, in turn, causes kinking of the ganglion cell axons as they pass through these plates. Kinking of the axons interferes with axoplasmic transport in both directions and as the neurotrophins and other supportive proteins from the brain cannot get to the cell body, the process of apoptosis is activated. Other consequences of kinking of the axons include depression of the cell survival gene, increased sensitivity of the cell to excitotoxins in the surrounding extracellular matrix, and an increase in reactive oxidative species (free radicals) (Fig. 2).

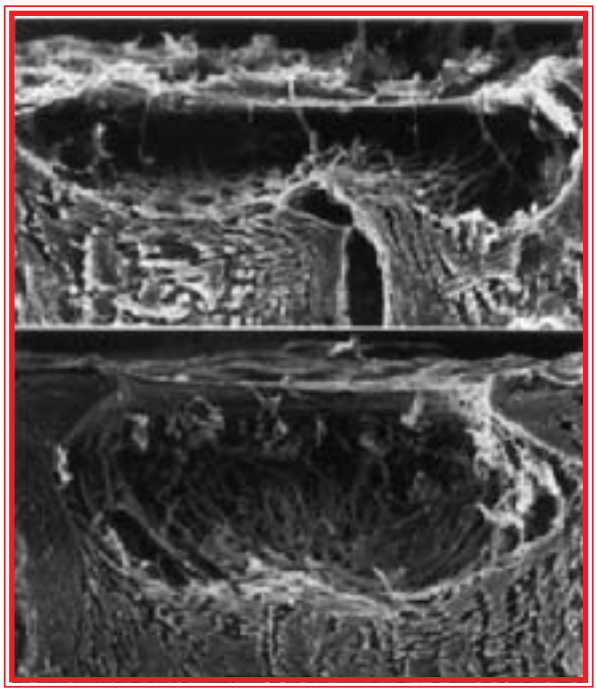


Fig. 2: Mechanical Damage to Optic Nerve.
The advanced damage by glaucoma causes collapse of the lamina cribosa. Lamina sheets become collapsed and malaligned. Ganglion cell axons are kinked and axoplasmic transport is blocked.

The Role of Chronic Ischemia

Deficient autoregulation in the vessels of the optic nerve area has been implicated in glaucoma. This could result in episodes of ischemia or a low level chronic ischemia either of which can lead to apoptosis (Fig. 3).

The Role of Cell Membrane Receptors and Calcium Channels

Cell membranes have receptors that are sensitive to such excitotoxins as n-methyl-d-aspartate and glutamate. These receptors open the calcium channels of the cell membrane and allow calcium to flood the cell. Calcium stimulates the cell oncogenes (BAD and BAX) to begin the apoptosis sequence. Calcium also interferes with mitochondrial and other intracellular functions disrupting the signal transport function of the ganglion cell.

Potential for Retarding Apoptosis

Inhibitors of glutamate or n-methyl-d-aspartate (NMDA) have been shown to retard apoptosis. Glutamate is found in higher concentrations in the vitreous of humans with glaucoma although it is not known if this is a primary (causative) phenomenon or a secondary one (due to death of cells releasing glutamate into the area of the optic nerve).

Nitric oxide also can trigger apoptosis. Nitric oxide is found in higher concentrations in the optic nerves of both rats and humans with glaucoma. An inhibitor of nitric oxide formation (aminoguanidine) has been shown to retard ganglion cell death in experimental glaucoma in rats.

As cells die some neurotoxic substances (like glutamate) are released into the surrounding extracellular matrix. These substances may trigger apoptosis in previously uninjured cells – a process known as secondary degeneration. Thus, any injury may be propagated beyond its original extent by secondary degeneration. NMDA inhibitors can slow or stop this process (Fig. 4).

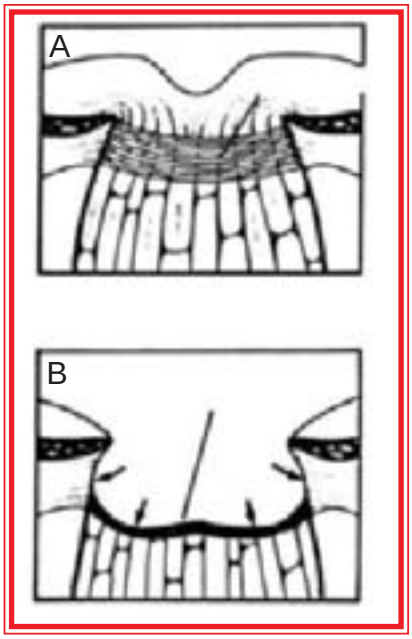


Fig. 3 A-B. Mechanical Damage to Optic Nerve.
Apoptosis is triggered by a variety of chronic processes including radiation, chemical, and mechanical injury that lead to ischemia. Observe the loss of tissue from a normal appearance (3-A) to an advanced stage of damage in the optic nerve fibers (3-B).

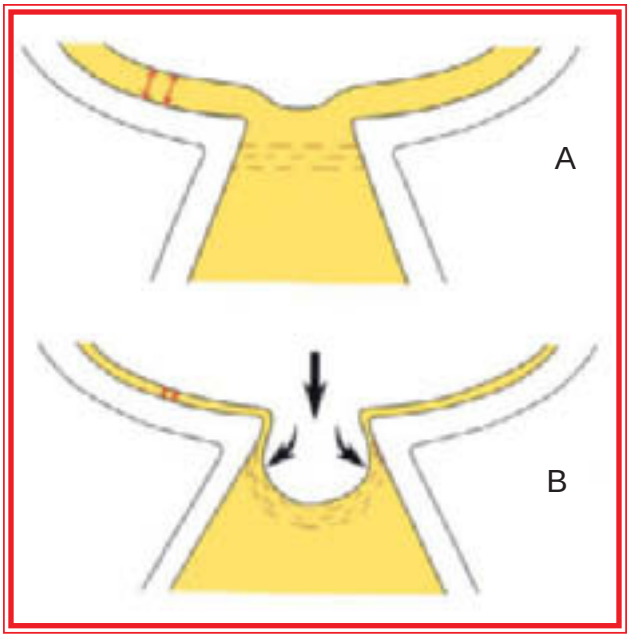


Fig. 4 A-B. Damage to Optic Nerve Fibers.
Other contributor causes of neural fibers damage are genetic influences, inmune mechanisms and the role of inhibitors of glutamate. In Fig. 4-A the thickness of the tissue and cup is symmetrically normal compared to the larger and deeper cup observed in Fig. 4-B (arrows).

Role of Genetic Influences

Genetics certainly plays a role in glaucoma. Those who carry certain mutations may be expected to develop glaucoma earlier in life, have a more progressive and aggressive course, or be more susceptible to optic nerve damage. Mutations in the myocillin gene, for example, make the trabecular meshwork cells more susceptible to damage from pigment and increased pressure; it is not unreasonable to expect that the same or similar mutations could make the ganglion cells more susceptible to injury from elevated intraocular pressure or promoters of apoptosis.

Role of Immune Mechanisms

Evidence is accumulating that immune mechanisms may play some role in the damage induced by glaucoma. Antibodies to heat shock proteins and autoantibodies are present in higher concentrations in patients with glaucoma compared to those who do not have it. Heat shock proteins have been shown to have a protective effect against cell stresses and a present in higher concentrations in early glaucoma. Inhibition of autoantibodies by injection of anti-autoantibody T cells or by vaccination with COP1 has been shown to slow or stop ganglion cell apoptosis in experimental glaucoma.

Keys to Management

It appears that damage to ganglion cells can occur through a variety of mechanisms including mechanical deformation, vascular insufficiency, genetic mutations, metabolic toxins, immune or autoimmune processes, and by secondary degeneration. In each patient, most likely, these mechanisms are at play in varying degrees and combinations. Teasing out the **details of these mechanisms is important as we change our paradigms from just lowering intraocular pressures to doing that plus protecting the optic nerve and ganglion cells from apoptosis.** Knowing the mechanisms at work will point out the ways that the nerve can be protected.

Chapter 13
DEVELOPMENT OF THERAPEUTIC VACCINES FOR GLAUCOMA

Michal Schwartz, Ph.D.

New Concept of Glaucoma

How to Protect Body Against Loss of Retinal Ganglion Cells

Glaucoma has traditionally been viewed as a disease associated with elevated intraocular pressure, and accordingly has been treated with antihypertensive drugs. However, the loss of retinal ganglion cells often continues to progress even when the pressure is reduced to normal. We suggested that **glaucoma should be viewed as a neurodegenerative amenable to neuroprotective therapy**.

Recently we discovered that one way in which the body copes with insults to nerves of the central nervous system is by harnessing the immune system to protect neurons from the damage caused by self-destructive compounds. On the basis of this and other observations, **we formulate a new concept of protective autoimmunity**. Using rats with glaucoma as a model, **we have demonstrated that vaccination with Cop-1**, an FDA-approved drug for the treatment of multiple sclerosis, **can protect against loss of retinal ganglion cells**. The experimental findings that led us to formulate the new concept, and to adopt vaccination as a therapeutic modality, are summarized here.

Glaucoma as Neurodegenerative Disease Amenable to Neuroprotective Therapy

Neuroprotection as Therapeutic Strategy – New Focus

The concept of neuroprotection as a therapeutic strategy for glaucoma has shifted the focus of therapeutic endeavor from external risk factors (e.g., increased pressure, vascularization, etc.) to internal factors (derived from the nerve itself.) Glaucoma has traditionally been regarded as a disease caused by elevated intraocular pressure (IOP). Several years ago, however, we suggested that glaucoma should be considered as a neurodegenerative amenable to neuroprotective therapy (Schwartz et al., 1996). This proposal was based on our observations that after an acute injury to the rat optic nerve, the loss of optic nerve fibers and cell bodies greatly exceeds the loss caused by the initial insult (Yoles and Schwartz, 1998a). We proposed that the observed propagation of damage is a result of secondary events caused by physiological compounds emerging in toxic quantities from the injured nerve fibers. In the case of glaucoma, we suggested that as in the case of acute

injuries, the nerve fibers and retinal ganglion cells that are damaged by the primary risk factor (such as elevated IOP) give rise to self-destructive factors that attack healthy neighboring neurons, thereby contributing to the spread of damage.

Landmark Observations

A number of observations may be considered as landmarks in shaping the view of glaucoma as a neurodegenerative disease amenable to neuroprotective therapy (Schwartz et al., 1996).

The Role of Increased IOP Alone

First, increased IOP has long been considered to be the most important risk factor in glaucoma. The reduction of IOP was therefore the treatment of choice in attempting to arrest or at least retard the propagation of optic neuropathy and the loss of retinal ganglion cells in glaucoma patients (Sugrue, 1989). However, many glaucoma patients continue to experience visual field loss even after therapeutic normalization of their IOP (Brubaker, 1996). In addition, many patients with glaucomatous damage show no evidence of elevated IOP, even on repeated testing (Liesegang, 1996). These findings suggested that, at least in some cases, increased IOP alone cannot explain the propagation of glaucomatous optic neuropathy, and that additional primary risk factors are involved.

The Presence of Substances Associated with Neuronal Degeneration

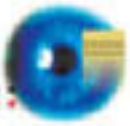
Second, it was recognized that as the disease progresses, the nerve itself contributes to the hostile conditions and hence to the pathogenesis of the disease. For example, abnormally high levels of glutamate and nitric oxide (both known to be associated with neuronal degeneration) were demonstrated in patients with glaucoma (Dreyer et al., 1996; Neufeld et al., 1997). This implied that therapeutic intervention should not be restricted, as in the past, to neutralization of the primary risk factors.

Hostile Environment to Neurons in Glaucoma

Third, it was acknowledged that ongoing changes in the extra- and intracellular milieu of the optic nerve induce in the neurons molecular changes that might affect their resistance (Caprioli et al., 1996) or susceptibility (Di et al., 1999) to the induced hostility. In this hostile environment, for example, neurons that are still viable might succumb to even a slight increase in glutamate toxicity. **Fourth**, it was suggested that molecular and cellular mechanisms that operate in other degenerative diseases may also be applicable to glaucoma (Neufeld, 1998). **Finally**, it was established that the death of retinal ganglion cells in glaucoma is a gradual process, involving intracellular changes that may be amenable to intervention (Quigley, 1999).

Progress in Glaucoma Therapy

Once glaucoma came to be viewed as a neurodegenerative disease, neuroprotection could be considered as a potential therapeutic strategy (Schwartz et al., 1996). Neuroprotective treatment includes neutralizing the mediators of toxicity (for example, by using glutamate receptor antagonists (Dreyer et al., 1997; Yoles et al., 1997; Levkovitch-Verbin et al., 2000; Yoles et al., 1999) or inhibitors of nitric oxide synthase (Neufeld et al., 1999); and increasing neuronal resistance to external or internal risk factors (McKinnon, 1997; Schwartz and Yoles,1999; Schwartz and Yoles,2000).



Amplifying Physiological Self-Repair Mechanism

In the course of our studies on injured optic nerves of adult rats (Yoles and Schwartz, 1998b), we recently came across another therapeutic possibility, which may be viewed as a way of amplifying a physiological self-repair mechanism that we found to be activated in response to central nervous system (CNS) insults (Yoles et al., 2001). The self-repair mechanism in this case operates externally to the optic nerve and is mediated by autoimmune T cells directed against central nervous system (CNS) antigens. In mammals this endogenous mechanism appears to be too weak to be effective; it was found, however, to be amenable to exogenous boosting. Our studies yielded the unexpected discovery that exogenous administration of T cells directed against the CNS self-antigen myelin basic protein significantly reduces the injury-induced spread of degeneration (Moalem et al., 1999; Schwartz et al., 1999). This process must be rigorously controlled, however, as without proper regulation it is potentially destructive to the tissue. We showed that this mechanism is not merely the result of therapeutic manipulation, but is a physiological mechanism in which the body harnesses the immune system in an attempt to defend the CNS against self-destructive components.

Protecting the Body from Own Self-Destructive Components

Until recently, the main function of the immune system was thought to be defense of the body against foreign pathogens. Our studies **revealed a new function of the immune system, namely to protect the body from its own self-destructive components**. Although initally received with much astonishment and not a little scepticism, this observation was a turning point in the perception of the immune response against self. It also suggested a novel approach to the search for effective treatment of neurodegenerative disorders, both acute and chronic (Moalem et al., 1999; Hauben et al., 2000; Kipnis et al., 2001; Yoles et al., 2001).

From the above studies we learned that autoimmunity, though a beneficial response designed to support the body after an insult, is too weak to provide an absolute defense against the self-destructive compounds emerging from damaged nerves (regardless of how the primary damage is caused). In our subsequent studies we attempted to: (a) determine whether all individuals are equally capable of manifesting this protective autoimmune response to injury; (b) understand the relationship between this "protective autoimmunity" and autoimmune disease; (c) identify the cells of the immune system that participate in protective autoimmunity; (d) unravel the mechanism underlying autoimmune protection; and (e) find a way to safely boost protective immunity in all individuals, or in other words, to enhance the body's own ability to manifest a protective autoimmune response without risking induction of an autoimmune disease. All of these questions were addressed over the last two years; not all of them have been fully answered (Kipnis et al., 2001; Schwartz and Kipnis, 2001a; Schwartz and Kipnis, 2001b). We showed that individuals differ in their ability to manifest protective autoimmunity after optic nerve damage, and that this ability is directly correlated with the resistance to development of an autoimmune disease development (Kipnis et al., 2001). All individuals can benefit, however, from the induction of protective autoimmunity by passive or active immunization, supporting our earlier observation that the spontaneous response is insufficient even in those individuals capable of manifesting it. It is possible that the endogenous response is sufficient for daily maintenance, when traumas to the nervous system are so minor that the individual may not even be aware of them, but that more severe trauma requires a stronger response. In an attempt to boost the response in a way that is therapeutically acceptable, the treatment should not carry any risk of of inducing an autoimmune disease.

Vaccination as a Therapy for Glaucoma

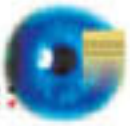
As discussed above, glaucoma has long been viewed primarily as a disease associated with increased IOP. Therefore, the models used for its study have been animals with an experimentally induced increase in IOP (Laquis et al., 1998), as their ocular characteristics are similar to those of patients with glaucoma. These models, like glaucoma patients, are characterized by the presence of well-known mediators of toxicity, such as abnormally high concentrations of glutamate and free oxygen radicals (Dreyer et al., 1996; Brooks et al., 1997).

Since the neuroprotective immune response found to operate under conditions of nonpathogenic damage is directed against self, it must be well controlled to avoid exceeding the risk threshold and inducing an autoimmune disease. Our studies have shown that whenever this risk exists, it is outweighed by the benefit. Recently, in seeking a way to elicit a risk-free anti-self response, we found that Cop-1 (a synthetic copolymer comprising the amino acids Ala, Lys, Glu, and Tyr), which is used as an immunosuppressive drug, can evoke passive or active T cell-mediated immunity that is neuroprotective (Kipnis et al., 2000). T cells specific to Cop-1, like T cells against self-antigens, were found to accumulate in the undamaged CNS. They might, therefore, represent cells that are cross-activated by CNS self-antigens in the damaged area, an activity which seems to be necessary for manifestation of neuroprotection. Unlike intact nerves, injured nerves allow the nonselective accumulation of T cells. However only T cells that recognize self-antigens are neuroprotective. The use of safe synthetic peptides that resemble self-antigens may provide a strategy for the development of safe anti-self immunity for neuroprotective purposes.

Cop-1 as a Vaccine

We examined the effect of Cop-1 used as a vaccine in three different models of optic nerve insult: (1) *Partial crush injury (acute injury) of the rat optic nerve*: In this model the spread of damage can be quantified, and some of the mediators responsible for it have been well studied. (2) *Glutamate-induced toxicity in retinal ganglion cells*: Glutamate is one of the major mediators of damage propagation in glaucoma and many other neurodegenerative disorders. (3) *Rats with intraocular hypertension*. In all of these models, vaccination with Cop-1 provided effective protection from degeneration . Moreover, in the case of increased intraocular pressure, protection by Cop-1 was successful under conditions where the pressure was kept chronically high. In the rat model of chronic ocular hypertension, vaccination with Cop-1 on the first day of pressure elevation was followed 3 weeks later by a reduction in retinal ganglion cell loss from about 30% to about 5% (Schori et al., 2001).

As Cop-1 is an FDA-approved drug for the treatment of a neurodegenerative disorder (multiple sclerosis), vaccination with this compound seems to be a promising approach. Being a remedy that harnesses the immune system, it has the advantage of promoting a continuous dialog between the remedial cells and the damaged tissue, thereby providing the tissue with whatever it needs for healing purposes. This type of therapy, being multifactorial, long-lasting, and self-controlled, may be viewed as boosting the body's own choice of therapy.



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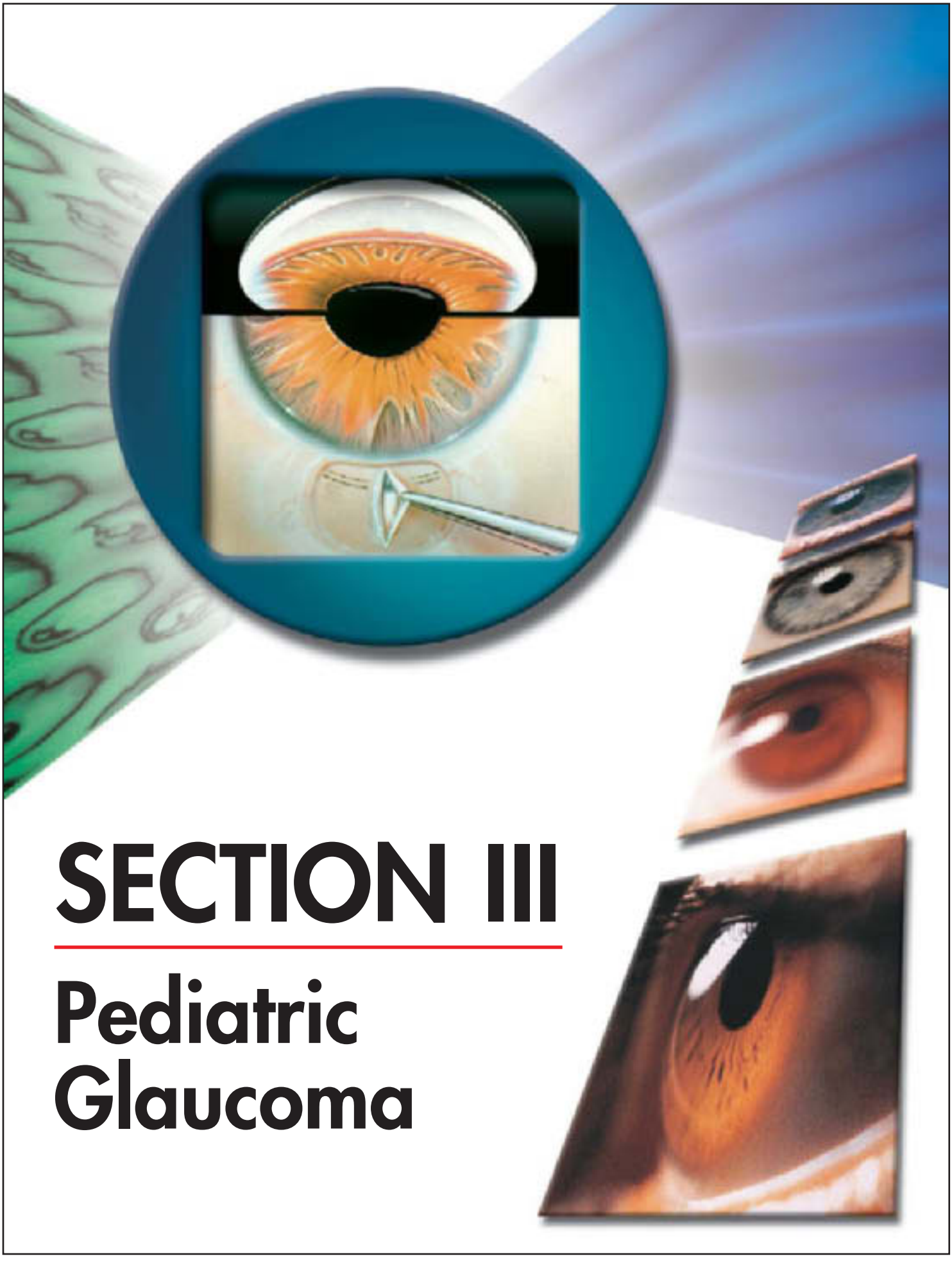
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SECTION III

Pediatric Glaucoma

Chapter 14
PEDIATRIC GLAUCOMA

Maurice H. Luntz, M.D., F.A.C.S.

Pediatric glaucoma may be congenital, infantile or juvenile (CIJ glaucoma), depending on the age of presentation. Congenital glaucoma presents in the first three months of life, infantile glaucoma between the first three months and three years of life, and juvenile between three and 35 years. The disease is related to developmental abnormality in the anterior chamber angle. When it presents in the first three months of life, or between the first three months and three years of life, there are often associated anatomic changes in the globe - in particular, enlargement of the cornea and the globe). When the presentation is after three years, there are generally no associated changes in the size of the globe. There may be a continuum between infantile and juvenile glaucoma, depending on the degree of anomalous development of the angle. Glaucoma presenting after 35 years of age is usually not related to developmental angle anomaly, but the angle appears normal and is considered to be an acquired-onset glaucoma. Late onset of juvenile glaucoma may occur either as a result of a developmental angle anomaly or an acquired disease of the angle, the clinical differentiation depending on gonioscopy. Late-onset juvenile glaucoma patients tend to have an angle resembling that in typical congenital glaucoma; in other words, there is a developmental angle anomaly. However, there may be a combination of both congenital and acquired components, so that the developmental anomalies with late-onset juvenile glaucoma may not be too striking. In acquired adult-onset glaucoma, the angle appears normal. An etiological relationship between juvenile glaucoma of the CIJ type and infantile glaucoma is further suggested by studies of pedigrees, which demonstrate cases of both infantile buphthalmos and juvenile glaucoma, as well as genetic studies.

CIJ glaucoma is an extremely uncommon condition, occurring in about one in 10,000 live births, but it may have a significant effect on vision. The most notable clinical feature is enlargement of the globe (buphthalmos), which occurs due to distension of the ocular coats as a result of raised intraocular pressure. Early on in the history of medicine, writers such as Hippocrates, Celsus and Galen recognized congenital enlargement of the globe, but they did not associate it with elevated intraocular pressure. They included buphthalmos in a single clinical entity of those conditions wherein the globe appeared to be of unusual size, including exophthalmos. In the 16th Century, Ambroise Pare (1573)[1] first used the term "ox-eye" to describe enlargement of the globe. The term ox-eye" was subsequently given the derivative buphthalmos. In 1722, SaintYves[2] attempted to classify the various forms of ocular enlargement and divided them into three groups: (1) the naturally large eye; (2) exophthalmos; and (3) increase in the size of the eye due to an abundance of aqueous humour. In 1869, von Muralt[3] and von Graefe[4] established buphthalmos as a form of glaucoma. They believed that the corneal enlargement was primary, and that the ocular hypertension resulted from damage to the corneal nerves. The distinction between physiologic enlargement of the eye or cornea and buphthalmos was established by Kayser (1914)[5], Seefelder (1916)[6] and Kestenbaum (1919)[7].

Hereditary Aspects of CIJ Glaucoma

The inheritance pattern for congenital glaucoma is autosomal recessive[8,9] but considered to be dominant for juvenile glaucoma. Glaucoma-related genes have recently been localized in congenital glaucoma. (See also "A Genetic Testing and Molecular Perspective on Glaucoma" Chapter 7 – **Editor**.) The genes so localized are as follows: the CYP 1B1 gene which is responsible for 80-90% of the cases studied, designated GLC 3A with a locus on the chromosome 2P 21.

Recently, a second locus on chromosome 1P 36 designated GLC 3B has been identified.

The major focus of glaucoma genetic research has been in juvenile open angle glaucoma. The first genetic location in this disease was identified as a result of a study of a North American family affected with autosomal-dominant juvenile glaucoma. The locus is referred to GLC 1A, and the gene was named TIGR (trabecular meshwork-induced glucocorticoid response)[10]. The TIGR gene (renamed the myocilin gene) is found in human trabecular meshwork cells, retinociliary body but not in the optic nerve. The penetrants of this type of glaucoma appear to lie somewhere 80 and 96%. More recent studies have demonstrated pedigrees of autosomal-dominant juvenile open-angle glaucoma not linked to the GLC 1A locus, suggesting that more than one gene is responsible for juvenile open-angle glaucoma.

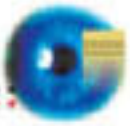
These genetic studies are ongoing and are important for early detection of carriers, of patients at risk of developing early-onset glaucoma, and, it is hoped, for treatment in the future. (See "A Molecular Perspective on Glaucoma, Section 1, Chapter 7).

Secondary Glaucoma in Childhood

In this chapter, CIJ glaucoma is cast as a primary ocular disease. However, glaucoma in a child may be secondary to other intra- or extra-ocular conditions, either due to disease in the anterior chamber angle other than developmental anomalies or, in some cases where the glaucoma arises from developmental anomalies of the angle which are part of a more generalized disease process. In these patients, the anomaly in the angle may be indistinguishable from that seen in primary congenital glaucoma. Included in children with secondary glaucoma are Marfan's syndrome, homocystinuria, Sturge-Weber disease (Fig. 1), von Recklinghausen's disease, Lowe's syndrome, aniridia, Axenfeld syndrome and Rieger's syndrome. Manifestations of the latter way present in the same patient as the Axenfeld – Rieger's syndrome with hypoplasia, iridogoniodysgenesis, maxillary, dental and umbilical abnormalities.



Fig. 1 A young adult with Sturge-Weber syndrome. An example of glaucoma secondary to more generalized malformation and characterized by a port wine stain of the face in the distribution of the V cranial nerve. The deformity may involve the angle, causing glaucoma. However, the more usual anomaly is one of the three groups described for CIJ glaucoma. Alternatively in rare cases glaucoma is due to increased pressure in the aqueous veins (increased episcleral pressure).



Pathogenesis

As indicated earlier in this discussion, CIJ glaucoma is associated with an anomalous development of anterior chamber angle. The prevailing theory of etiology until 1955 was the presence of abnormally persistent mesodermal tissue in the angle, interfering with its function. This tissue presented as truly membranous structure and was known as Barkan's membrane[11]. Surgical cure was believed to result from incision of this tissue, allowing access of aqueous to Schlemm's canal.

In 1955, however, Allen, et al[12] proposed that the angle was formed by a simple splitting of two distinct layers of mesodermal tissue. The anterior layer formed the trabecular meshwork, while the posterior layer formed the iris and ciliary body. They attributed some cases of developmental glaucoma to failure of complete cleavage of the angle structures. This resulted in persistence of mesodermal tissue which failed to resorb in the usual way. More recently, it has been suggested that the residual tissue noted in the angle in developmentally abnormal angles is derived from neuroectoderm rather than from mesoderm.

Clinical Manifestations

Prevalence

As previously mentioned, the disease occurs in one in 10,000 live births. Though a relatively rare disease, it is important, as it constitutes a significant percentage of the causes of blindness in children.

Bilateral Disease

The majority of cases are bilateral, occurring approximately twice as often as unilateral cases.

Sex Incidence

The disease occurs more frequently in males, with a male preponderance of 58.9% to 71% of cases.

Symptoms

The symptoms are photophobia, epiphora and blepharospasm. Any child presenting with one of these symptoms should be suspected of having congenital glaucoma.

Photophobia results from corneal epithelial edema related to increased intraocular pressure. Photophobia can be confirmed by bringing the infant into a dark room, observing the child as the lights are switched on. The child will immediately close his/her eyes.

Blepharospasm and epiphora are similarly the result of corneal edema.

Diagnostic Clinical Signs

Evaluation of a child suspected of having CIJ glaucoma requires sedation or general anesthesia. Generally, children can be adequately sedated with sedative suppositories, but if this does not adequately sedate the child a general anesthetic is necessary. Attention is first paid to intraocular pressure. It can be evaluated with a hand-held applanation tonometer or the Schiotz tonometer. If the child is under a general anesthetic, the intraocular pressure will generally read 3-4mm lower than the intraocular pressure in the child while awake.

Corneal Evaluation

The most obvious clinical feature is corneal edema. Initially, epithelial edema may progress to involve the stroma if intraocular pressure is not treated. Long-standing stromal edema may result in

permanent corneal opacity. Breaks in Descemet's membrane occur as a result of increased intraocular pressure and stretching of the cornea. These tend to be horizontally oriented if central, and concentric when occurring at the limbus. They are known as Haab's striae and are best viewed on the slit lamp by retroillumination.

Corneal enlargement (buphthalmos) (Fig. 2) is another striking clinical feature. It is a direct result of the effect of raised intraocular pressure on the external ocular coat. In general, the cornea and sclera will not stretch after the child has reached three years of age.

The normal corneal diameter in infants is 8-10mm, and the horizontal diameter is 0.5mm longer than the vertical. At the end of the first year, the diameter may reach 11.5mm. Any measurement greater than 12mm suggests buphthalmos. However, a normal-sized cornea does not exclude the diagnosis, and other clinical signs must be taken into account. Aggressive corneal enlargement is a definite sign of congenital glaucoma, and, if it occurs following surgical treatment, it suggests inadequate reduction of intraocular pressure. Buphthalmos must be differentiated from megalocornea (a physiologically enlarged cornea). In megalocornea there is no corneal edema and no progressive enlargement.

In addition, the cornea in buphthalmos undergoes peripheral thinning. In the late stages, the cornea becomes permanently scarred.

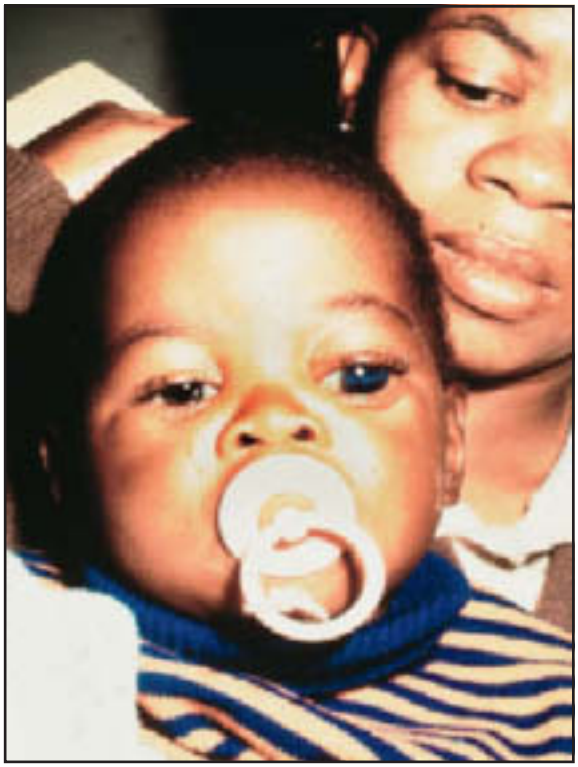
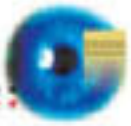


Fig. 2 A child with buphthalmos O.S. and a normal-appearing eye O.D.

Anterior Chamber Depth and Axial Length Measurements

The anterior chamber is characteristically deep, reaching as much as 7.3mm in depth.

The entire globe is enlarged in long-standing cases. Measurement of axial length using ultrasound is helpful for diagnosis and follow-up. In newborns and infants, axial length does not exceed 18mm. By six months, it reaches 20mm. Measurements in excess of these numbers suggests congenital glaucoma.



Changes in Refraction

The enlargement of the cornea, the increased depth of the anterior chamber and enlargement of the globe may lead to alteration of the refractive state. Progressive myopia is an indication of increasing axial length. However, myopia is counteracted by other factors - in particular, flattening of the corneal curvature and lens due to stretching of the ciliary body, as well as increasing depth of the anterior chamber.

Optic Nerve Head

The optic nerve head is susceptible to glaucomatous cupping secondary to increased intraocular pressure. This may occur relatively early in the course of the disease. It is uncertain if distensibility of the anterior portion of the sclera and cornea protects the nerve as a result of raised intraocular pressure. In the infant, optic nerve cupping is reversible if intraocular pressure is controlled. Therefore, optic nerve damage can be prevented with early diagnosis and aggressive treatment.

Anterior Chamber Angle

The appearance of the angle in CIJ glaucoma is crucial for evaluation of the etiology and the prognosis for surgery. However, an abnormal angle is not sufficient for the diagnosis of CIJ glaucoma but must be considered along with the other signs and symptoms already described. Typical angle anomalies may be absent in some cases of CIJ glaucoma, or it may be present as a finding without other evidence of the disease.

The angle in the newborn is not fully developed. The most recognized finding in the newborn angle is the presence of a thin, delicate tissue covering the angle structures. Furthermore, the uveal meshwork may be more abundant in the newborn angle than in the adult. The thin membrane covering the angle in the normal newborn will be fenestrated and open and is difficult to recognize gonioscopically. Schlemm's canal will fill with blood when pressure is applied with the gonioscope.

In infantile glaucoma, the angle differs significantly from the normal angle in the newborn. The angle anomaly in the glaucomatous eye may be asymmetric between the eyes and may not involve the entire circumference of the angle. These angle anomalies fall into three major groups, which are of major importance in the diagnosis of the disease and in the prognosis for surgical management. These groups were described by Luntz in 1979[14] and Hoskins in 1983[15]. Both classifications describe the same angle anomalies, but from different viewpoints. In the Luntz classification, the angle anomalies are described based on interpretation of the abnormal tissue in the angle, and the Hoskins classification is based on the anatomic location of the abnormal tissues in the angle.

Group I - Presumed Mesdermal Anomaly of the Angle (Luntz) or Trabeculodysgenesis (Hoskins)

This constitutes the commonest anomaly seen in children with CIJ glaucoma, accounting for approximately 73% of eyes. Pigmented tissue which should not be present is noted in the angle and blocks the trabecular meshwork. This pigmented tissue is interpreted as constituting remnants of mesoderm which has not resorbed during development. This presumed mesoderm may present as a continuous sheet, stretching from the iris root across the ciliary body, across the trabecular meshwork and to Schwalbe's line, covering the entire 360° of the angle it may present as clumps of pigmented tissue



Fig. 3. Presumed mesodermal anomaly of the angle (trabeculodysgenesis). The posterior corneal surface appears normal. This is visible in the uppermost portion of the illuminated circle. The trabecular meshwork zone lies approximately in the center of the illuminated circle and is characterized by darkly pigmented bands, presumably mesoderm, lying on the trabecular meshwork and scattered aggregates of the same darkly pigmented tissue at each side of the slit lamp beam. This tissue is lying on the root of the iris and over the trabecular meshwork. The peripheral iris surface is evenly illumination by the light of the slit lamp beam, indicating that it is flat and not involved in the developmental anomaly. This is an important point to appreciate, because it indicates that there is no cicatricial component on the iris surface. The center of the peripheral iris surface is a round,brown nodule, which is a benign iris nevus.

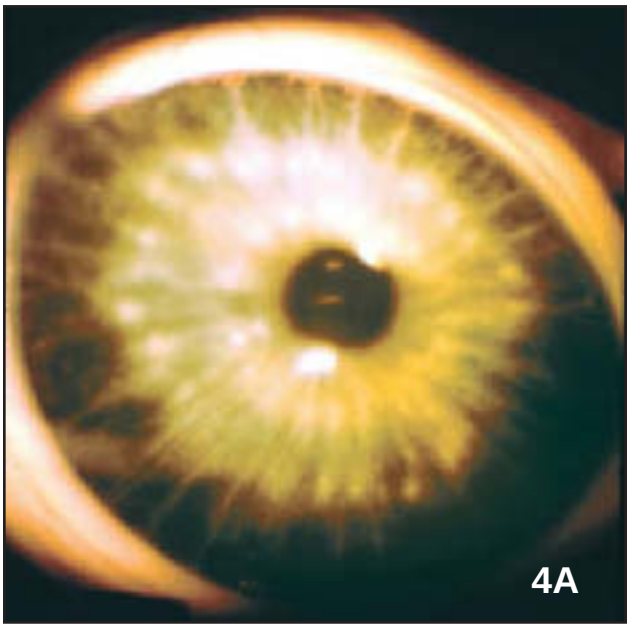
distributed over the surface of the angle (Fig. 3). In another variant, the iris root inserts in the angle in front of the ciliary body, and not behind it as is usual, and the pigmented tissue is broken into fine processes (iris processes) lying across the trabeculear meshwork.

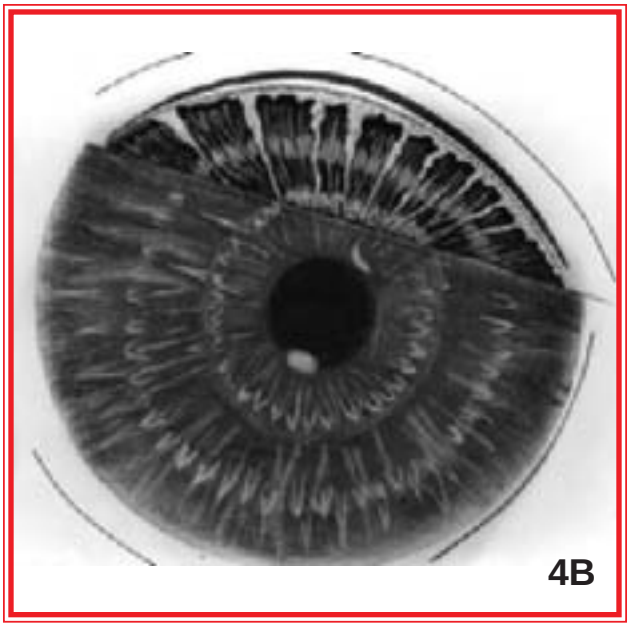
Throughout this group, there is no evidence of any abnormality of the iris periphery. The surface of the iris is flat and normal in appearance; there is no undulation or other abnormality of the iris surface. This is the basis for the Hoskins' classification of this group as trabeculodysgenesis and is a major point of differentiation from the other two groups. When studied through the slit lamp, the iris surface is evenly illuminated with the slit lamp focused on it and appears to be of normal structure and consistency.

Group II - Cicatrized Angle (Luntz) or Iridotrabeculodysgenesis (Hoskins)

This group of angle anomalies is characterized by structural changes involving the trabecular meshwork and the anterior surface of the iris root, suggesting that a cicatricial process has occurred. The prognosis for surgery in these angles is considerably worse than those described in the preceding group. On gonioscopic examination, the trabecular meshwork area is characterized by a light brownish-colored membrane at its base (junction with the iris root). The upper peripheral edge of this membrane is straight and attached to the base of the trabecular

meshwork, whereas the lower or free edge which reaches the iris periphery has a serrated contour and develops a number of small projections, each of which extends downward onto the surface of the iris root, forming radial iris folds. Between these radial folds, the iris surface forms a trough which lies in a plane deep to the radial fold. This abnormality of the iris extends only in the area of the iris root. If the slit lamp beam is focused on the radial fold of the iris, the iris tissue between the folds is posterior to the slit lamp beam and out of focus. This suggests that the radial folds have been pulled anteriorly by the projections of the brown-colored membrane over the trabecular meshwork, and this suggests a cicatricial process (Figs. 4a and 4b).





Cicatricial Angle Anomaly (Iridotrabeculodysgenesis)

Fig. 4a A light brownish membrane is present at the base of the trabecular meshwork. (™) The upper edge of this membrane is straight and fades into the TM, the lower, free edge reaches the iris periphery, has a serrated contour and develops a number of small projections, each one of which extends onto the surface of the iris root, forming radial iris folds. Between these radial folds, the iris surface forms a trough which lies in a plane deep to the radical fold. This abnormality of the iris extends only in the area of the iris root. When the slit lamp beam is focused on the radial iris folds, the iris tissue between the folds is posterior to the slit lamp and out of focus.

If the iris were cut in cross-section, the iris surface would undulate, the radial folds lying anterior to the troughs between the radial folds. This irregular appearance of the iris surface is believed to be the result of a cicatricial process affecting the angle during its development. In these cases, the entire limbal area is involved, because Schlemm's canal is found closer to the limbus, situated 0.5mm to lmm behind the surgical limbus, instead of the usual position 2.5mm behind the surgical limbus. The prognosis for trabeculotomy in this type of angle anomaly is poor, with a success rate of about 30%.

Trabeculectomy or combined trabeculectomy/trabeculotomy is the surgery of choice. This second group is termed "iridotrabeculodysgenesis" in the Hoskins classification.

Fig. 4b. A drawing of the cicatricial angle anomaly in Fig. 4a.

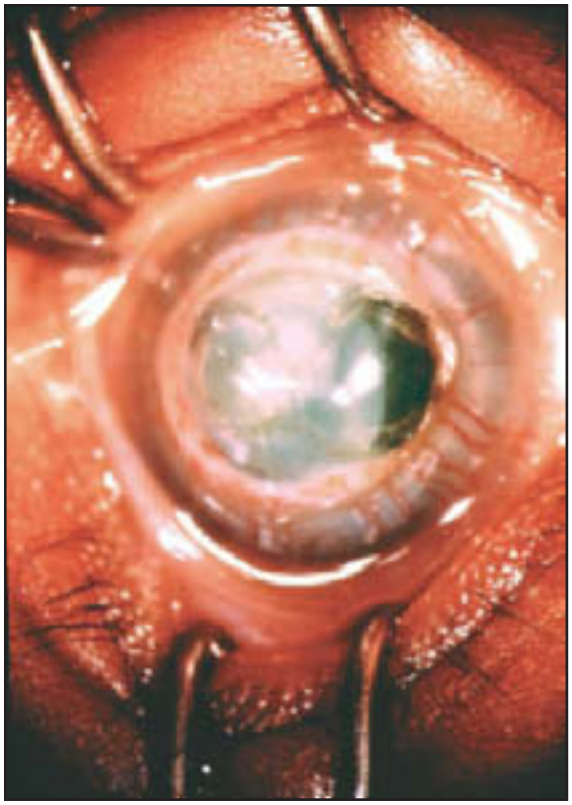


Fig. 5. Advanced iridocorneal dysgenesis. The cornea is scarred, and the iris and lens are adherent to the posterior corneal surface. The prognosis for trabeculotomy is poor.

In the Hoskins classification, this group III is labelled "iridocorneal dysgenesis." This particular eye is an example of Peter's anomaly.

Group III - Iridocorneal Dysgenesis (Luntz and Hoskins)

This group is characterized by varying degress of angle iridocorneal dysgenesis from mild to severe and presents within the first few weeks of life. The characteristic clinical features are central corneal opacification, prominence of Schwalbe's line, which may be anteriorly placed and visible in the corneal periphery, with varying degrees of anterior segment malformation. (Fig. 5) In severe cases, there are adhesions between the iris surface at and adjacent to the pupil, the lens capsule or the posterior cornea (Fig. 6).

This group has a poor prognosis for surgery, similar to the eyes in the cicatrized group.

Management of CIJ Glaucoma

The treatment of CIJ glaucoma is surgical, with the objective of reducing intraocular pressure to normal levels (mid- to upper teens). Two operative procedures are in general use: trabeculotomy and goniotomy. However, in the cicatricial angle and the iridocorneal dysgenesis groups, the prognosis for surgery with either of these procedures is poor, and in these cases a combined trabeculotomy/trabeculectomy gives better results.

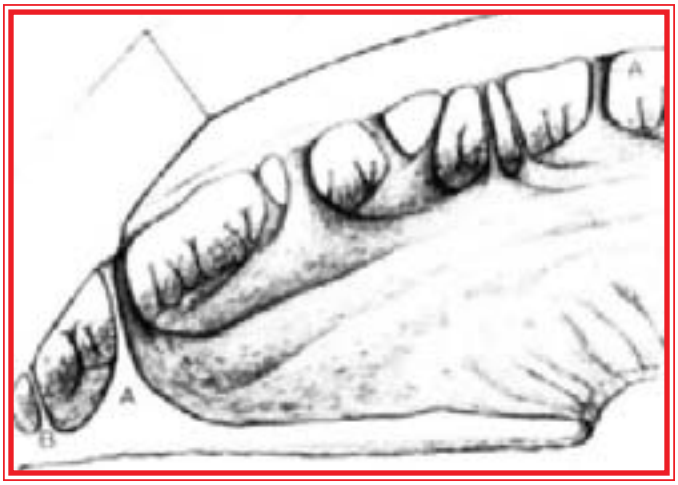


Fig. 6. An artist's interpretation of iridocorneal dysgenesis as seen gonioscopically. The anomaly involves the peripheral iris which is divided into processes adherent to the posterior corneal surface, and may also involve the pupil margin and the lens.

Preoperative Patient Preparation

Anesthesia

The procedure is generally done with general anesthetic.

Skin Preparation and Exposure

After anesthetizing the child, the operative field is prepared using antiseptic solution (e.g., Betadine), followed by the surgeon's usual prepping and draping procedures.

The operative procedure is a microsurgical procedure, and an ophthalmic surgical microscope is placed in position.

Surgical Technique for Trabeculotomy

Conjunctival Flap (5x magnification)

The operation is commenced by raising a fornix-based conjunctival flap 7mm wide at the limbus. Tenon's fascia and episclera are removed, and the sclera is exposed and cleaned. A triangular portion of sclera is exposed, measuring at least 3mm from base at the surgical limbus to its apex. (Fig. 7).

Scleral Dissection (10x magnification)

Using a 15° superblade or a diamond knife, an incision is made through half the scleral depth, extending from the surgical limbus at the midpoint of the base of the exposed sclera and running radially and posteriorly for 3mm (Fig. 7). With one edge of this incision held with forceps, the incision is rotated outward, allowing greater visibility, and the scleral incision is deepened until bluish tissue in the anterior half of the incision becomes visible which represents an external anatomical landmark for deep corneal lamellae and trabecular meshwork. The incision is then undermined on each side using a 15° superblade to increase the surgical exposure (Fig. 8).

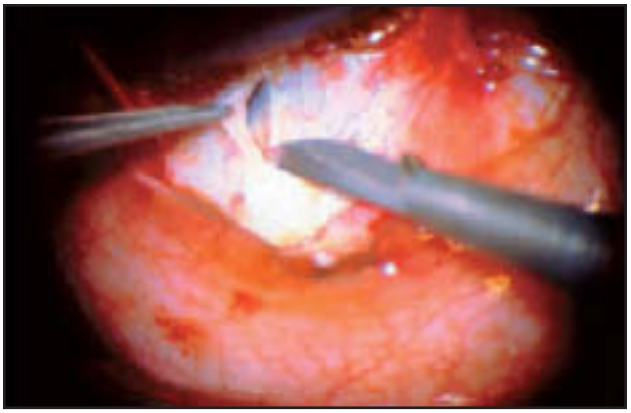


Fig. 7. Technique for trabeculotomy. A radial incision, extending from the surgical limbus posteriorly for 3mm, is cut in the sclera and dissected until the landmarks of the deeper structures are just visible. These landmarks are, superiorly, the lighter blue deep cornea lamella, inferior to it a grayish band of trabecular meshwork tissue, and inferior to that the white scleral tissue. They are clearly seen in the illustration.

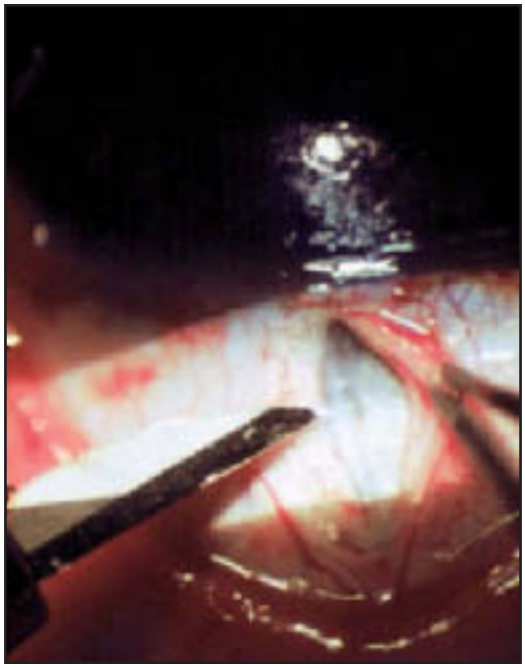


Fig. 8. Technique for trabeculotomy. The radial incision is undermined on each side to improve exposure of the deeper tissue. The surgical landmarks are easily visible in the illustration. The junction of the posterior border of the trabecular meshwork band and the sclera is the external landmark for the scleral spur, and the landmark for Schlemm's canal indicated by the point of the knife.

The external surgical landmarks are now more visible (Figs. 7 and 8), and the surgery proceeds to the next step, which is dissection of the external wall of Schlemm's canal. To locate Schlemm's canal, the surgeon needs to visualize the surgical landmarks and recognize the different tissues represented by these landmarks (Figs. 7 and 8). Starting from the surgical limbus and following the radial incision posteriorly, one first notes a bluish transparent looking tissue which represents deep corneal lamellae. Posterior to the deep corneal lamellae, the next structure is a band of grayish, less transparent tissue which represents the trabecular meshwork. Posterior to this band is white, dense, opaque scleral tissue. The junction of the lower limit of the trabecular meshwork band and the white scleral tissue represents the surgical landmark for the scleral spur, and it is in this area that Schlemm's canal is found indicated by the knife point in Fig. 8. In most eyes, the canal lies 2-2.5mm behind the surgical limbus.

Dissection into Schlemm's Canal (15x magnification)

A vertical incision using a microblade (either a 15° superblade or a 75 Beaver blade or diamond knife), a radial incision is made at the junction of the lower margin of the trabecular meshwork and the scleral tissue (Fig. 8).

This incision is carefully deepened until it is carried through the external wall of Schlemm's canal, at which point there is a gush of aqueous and occasionally aqueous mixed with blood. The dissection is continued through the external wall until the inner wall of the canal is visible. The inner wall is characteristically slightly pigmented and composed of criss-crossing fibers (Figs. 10 A-B). Once this point is reached, the lower blade of a Vannas scissors is passed into the canal through the opening in the external wall, and a strip of the external wall of the canal is excised (Fig. 9). The canal is unroofed for

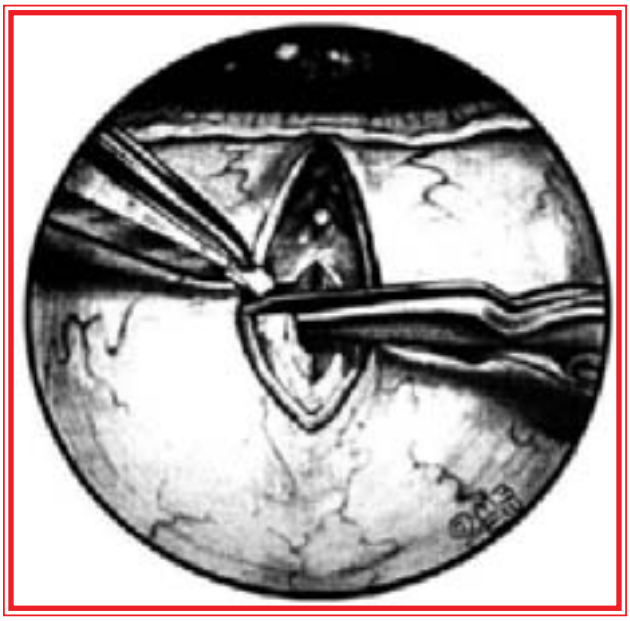


Fig. 9. Technique for trabeculotomy. A diagramatic representation of unroofing the outer wall of Schlemm's canal. The outer wall has been dissected open by a radial incision. One blade of a Vannas scissors is introduced into the lumen of the canal through this radial incision, moved along the lumen. The outer wall of Schlemm's canal is dissected for 1-1.5mm on each side. In this way, a portion of the lumen of Schlemm's canal and the inner wall are exposed.

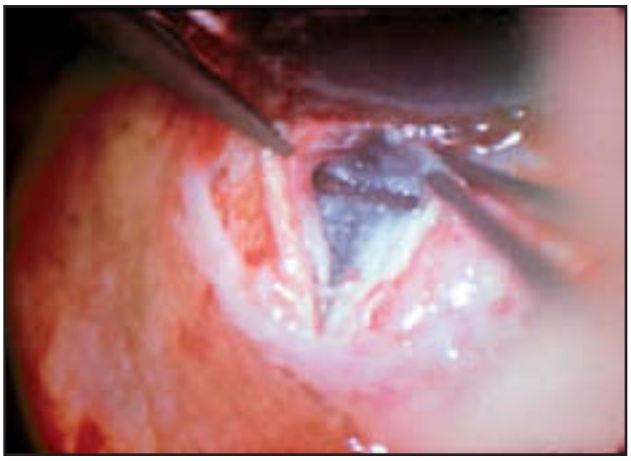


Fig. 10-A. Technique for Trabeculotomy.

In this photograph, one is looking directly at the lumen of Schlemm's canal and the internal wall of the canal, which is characteristically darkly pigmented. This follows unroofing of the canal with Vannas scissors, as demonstrated in Fig. 9. Above the canal, one can see the blue deep corneal lamellae, and inferior to the canal is the white scleral tissue.

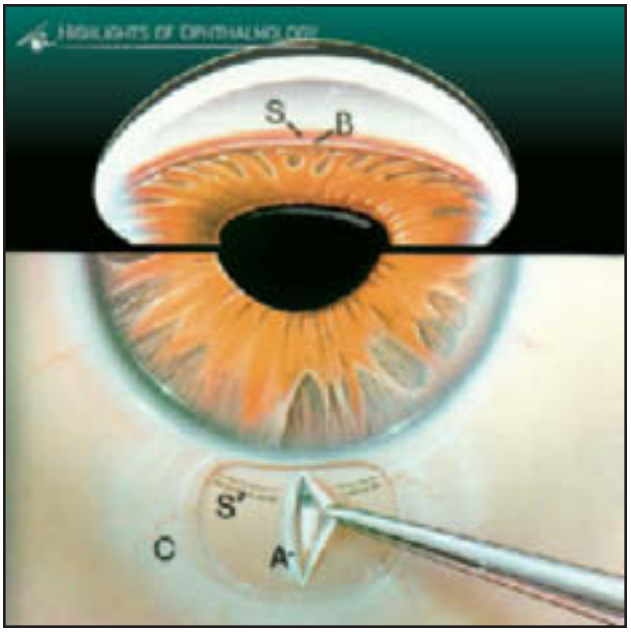


Fig. 10-B: Trabeculotomy for Congenital Glaucoma - Gonioscopic and Surgeon's Views

The surgeon's view (lower figure) shows a fornix-based conjunctival flap (C) already performed. A 3mm long radial incision extending from the limbus posteriorly in the sclera is created. This slit incision (A) is dissected through the sclera to Schlemm's canal (S-dotted line). The gonioscopic view above shows the location of the pigment band (Schlemm's canal - S) and scleral spur (B).

1-1.5mm circumferentially (Figs. 9 and 10 A-B). The inferior blade of the Vannas scissors introduced into the canal should enter the canal with ease and slide easily along the canal. If the blade does not enter easily, it indicates that the external wall of the canal has not been adequately dissected into the lumen, and if one pushes the blade a false passage may be formed.

Introduction of Trabeculotomy Probe (5x magnification)

A trabeculotomy probe of the design shown in Fig. 11 (Luntz trabeculotomy probe) is introduced into the canal. Other designs for trabeculotomy probes have been described by Della Porta, Lee Allan, Harms, Dobree. The Luntz probe has an inferior blade of 0.20mm in diameter, which fits snugly into the canal; the upper blade runs over the limbus and is kept resting on the cornea, ensuring that the lower blade rotates through the inner wall of the canal in front of the iris and behind the cornea and does not create a false passage. The two blades are separated by l mm. The shaft of the probe is divided into three segments, so that the central third can be stabilized with the left hand, while the right hand rotates the upper third of the shaft, which, at the same time, will indirectly rotate the lower third of the shaft



Fig. 11. Technique for Trabeculotomy.
A Luntz trabeculotomy probe, showing the 0.2mm diameter inferior blade, which is separated from the superior thicker blade by 1mm. The inferior blade enters the canal. Fingers hold the middle third and upper third of the shaft.

and the blades (Figs. 11 and 12). This method avoids up or down movement of the probe tip which could disrupt the corneal lamella or the iris.

The probe is passed along the canal to one side and rotated into the anterior chamber, rupturing the inner wall of the canal and also rupturing mesodermal tissue lying on the trabecular meshwork, thus opening the inner wall of the canal to the anterior chamber and the aqueous (Figs. 12 A-B). The same process is repeated on the other side. The probe is

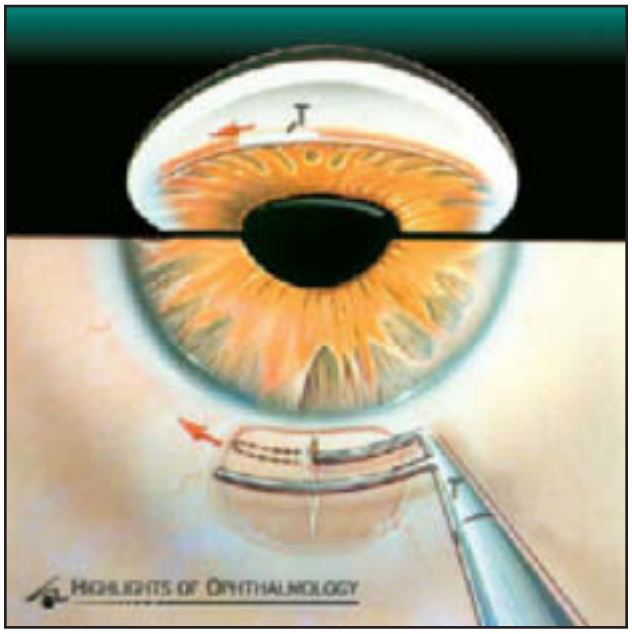


Fig. 12-A: Trabeculotomy for Congenital Glaucoma - Gonioscopic and Surgeon's Views
A trabeculotome (T) being threaded (arrow) into Schlemm's canal as far as possible. The external probe shows the position of the internal probe as it is threaded within the canal. The gonioscopic view above shows the trabeculotome probe (T) within the canal.

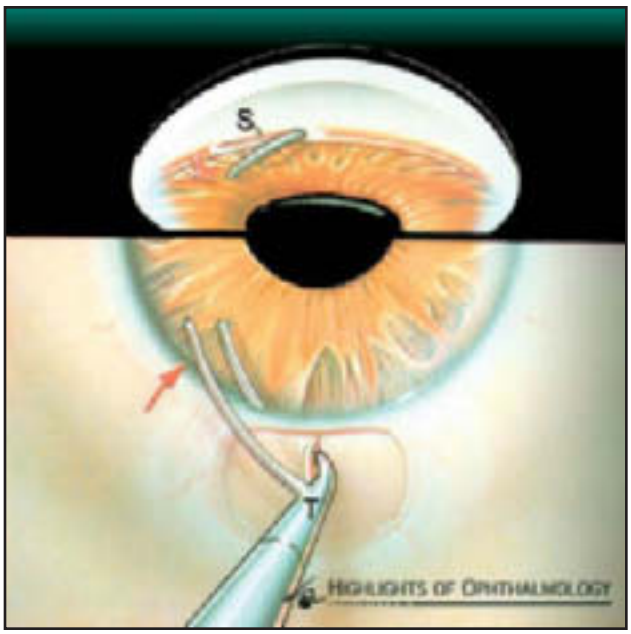
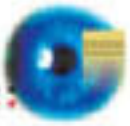


Fig. 12-B: Trabeculotomy for Congenital Glaucoma - Gonioscopic and Surgeon's Views - Internal Opening of Schlemm's Canal
The trabeculotome (T) is rotated (arrow) to rupture Schlemm's canal and the trabecular meshwork. The gonioscopic view above shows the probe being rotated into the anterior chamber as Schlemm's canal (S) is opened internally. The same procedure is performed for the right hand side (not shown).



then withdrawn, and, if the procedure has been adequately performed, a bridge of the inner wall of Schlemm's canal remains intact between the two sides. This bridge prevents iris prolapse into the surgical incision, so that peripheral iridectomy is not necessary. However, if iris does prolapse into the incision, a peripheral iridectomy should be performed.

It is most important that the probe is introduced into the canal without using force to avoid creating a false passage. If the probe will not slip easily into the canal, it implies that the canal has not been adequately opened by removing all fibers of the external wall. If this occurs, the probe is withdrawn, the dissection of the outer wall is continued using a sharp microblade until the surgeon is satisfied that all fibers of the outer wall have been removed.

The anterior chamber should be present at all times during the procedure. There may be a little intracameral bleeding from the inner wall as the probe passes into the anterior chamber, disrupting the inner wall of the canal. As the probe swings from the canal into the anterior chamber (Figs. 12 A-B), the surgeon should carefully watch the iris for any movement of the iris. Movement of the iris implies that the probe is catching the iris surface, and this may result in an iridodialysis. If this occurs, the probe should be immediately withdrawn without continuing its entry into the anterior chamber and replaced, keeping the tip of the probe slightly anterior, so that it does not rupture the inner wall prematurely. At the same time, the cornea is carefully monitored to ensure that the probe does not rip through cornea and Descemet's membrane. Disruption of the cornea is easy to detect, because small air bubbles will appear in the cornea. If this occurs, the probe should be removed and repositioned.

The important point is that the probe should enter the canal with ease and slide along the canal without the use of force.

Some surgeons prefer to perform trabeculotomy under a lamellar scleral flap. This technique is described later under "Surgical Technique for Trabeculectomy/Trabeculotomy."

Closure of the Incision (5x magnification)

Closure of the incision is achieved with three 9-0 vicryl or 10-0 nylon sutures in the scleral incision, and the conjunctival flap is rotated anteriorly to the limbus and secured with one 10-0 nylon suture at each edge of the incision.

Postoperative Monitoring

It is essential to provide careful postoperative monitoring. Blood in the anterior chamber should absorb by the first or second postoperative day. The cornea should remain clear, and there is minimal iritis. An antibiotic/ steroid eyedrop is used postoperatively for 3-4 days.

The child should be re-examined after six weeks, at which time intraocular pressure is measured, as well as corneal diameter, and gonioscopy is performed. Gonioscopically, a cleft is visible at the site of the trabeculotomy, situated just anterior to the iris root. Pressure at the limbus with the gonioscope may result in a retrograde flow of blood along Schlemm's canal which escapes through the ruptured inner wall at its junction with the intact inner wall. When it occurs, this is good evidence that the trabeculotomy is functional. Subsequent examination

should be performed at three months and six months and, after that, at yearly intervals. Any recurrence of increased intraocular pressure or increase in corneal diameter or increase in the cup-disc ratio indicates a need to repeat the trabeculotomy procedure at a different site.

Complications of Trabeculotomy

Trabeculotomy is a safe procedure, and there are few complications.

1. Post-operative hyphema. This is not unusual but generally resolves within a few days. Persistent bleeding occurs only if the iris root has been torn by the trabeculotomy probe, producing an iridodialysis.

2. Flat anterior chamber. This is a rare complication and is usually associated with pupillary block, relieved by cycloplegics. If not reversed, the AC may require reformation in the operating room.

3. Traumatic iridodialysis and tearing of Descemet's membrane are preventable, as described above.

4. Staphyloma of the sclera may occur due to inadequate suturing of the scleral incision.

5. Failure to find Schlemm's canal. Absence of Schlemm's canal is a rare anomaly. The canal is consistently located from 2-2.5mm posterior to the limbus, unless the angle has a cicatricial component. If the latter case, the canal is found closer to the limbus. In large buphthalmic eyes, the canal may be collapsed and difficult to identify. In these difficult cases, careful dissection within the plane of the trabecular tissue, dissecting from the limbus posteriorly for 2.5mm will usually locate the canal somewhere in this area. Even when the canal is collapsed, the inner wall can be identified by its characteristic appearance of pigmented, criss-crossing trabecular meshwork fibers.

Surgical Technique for Goniotomy

A gonioscopy lens is selected (Fig. 13 and 15) and attached to the surface of the cornea.

Worst Lens (Fig. 13)

This is a popular lens. It fits around the limbal area with a flange extending onto the perilimbal conjunctiva. The flange is perforated by four openings, which allow the lens to be sutured to the perilimbal episcleral tissue with 7-0 sutures. The lens has an oval port that permits entry of the goniotomy knife. Once secured to the conjunctiva, the lens straddles the cornea and provides a 2x magnification of the angle.

The operating microscope used in conjunction with the Worst lens is used at relatively low magnification in order not to lose resolution through overmagnification. The Worst lens is connected through a cannula and a polyvinyl chloride (PVC) tube to a syringe or infusion set containing balanced salt solution. The interior of the lens is filled with balanced salt solution to form a fluid bridge between the cornea and the inner surface of the lens. The lens is positioned so that the port through which the knife is introduced is at a convenient spot, if possible facing the temporal side.

Barkan and Lister Lenses (Fig.13)

The Barkan and Lister lenses are hand-held on the cornea and allow viewing of the angle with the operating microscope in a vertical position. The inferior surface of the goniotomy lens is spherical, with a steeper curvature than the corneal curvature. The space between the corneal surface of the goniotomy lens and the cornea becomes a part of the lens system when filled with balanced salt solution. As these lenses are hand-held and need to be rotated to obtain a view around the angle, it is difficult to maintain this saline meniscus between the lens and cornea. For this reason, the Lister lens has been modified with the attachment of a fine silver cannula attached to a PVC tube which, in turn, is attached to a balanced salt infusion set. Notwithstanding these modifications, it is difficult to visualize the angle adequately and to maintain an air-bubblefree lens-corneal compartment. Furthermore, breaks in Descement's membrane, scars in the cornea and thickening of Descemet's membrane may all result in refractile edges that impair the resolving power of the gonioscopic lens system, further reducing visibility.

The need to use a multiple lens system (operating microscope, gonioscopy lens, lens-cornea-fluid meniscus and cornea) to visualize the angle and the above-mentioned changes in the cornea which reduce visualization all combine to make goniotomy a difficult and hazardous procedure, bearing in mind that a sharp instrument (goniotomy knife) crosses the anterior chamber. These prismatic gonioscopy lenses usually require tilting of the operating microscope, and this further reduces its resolving power.

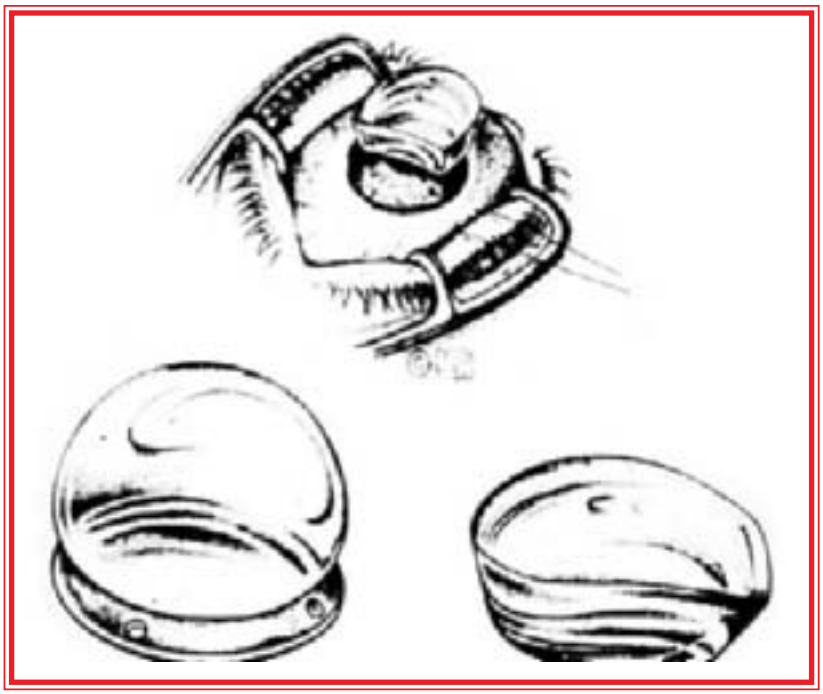


Fig.13. Line drawings illustrating, superiorly, an eye with a Barkan lens in place on the cornea; inferiorly and left, the Worst lens; and inferiorly and right, the Barkan goniotomy lens.

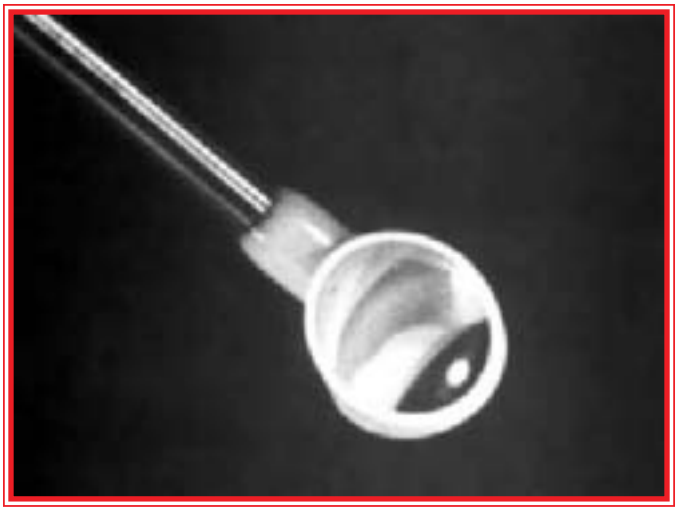


Fig.14. The Swann-Jacob goniotomy lens. The posterior corneal surface of the lens is convex and has a curvature which is flatter than the corneal curvature. The lens has a metal handle which allows manipulation of the lens without obstructing the operative field.

Swann-Jacob Lens (Fig. 14)

Swann has addressed this problem and designed a gonioscopy lens with a convex anterior surface, allowing observation of the angle with the microscope vertical to the cornea, which reduces distortion. The lens is small and fits snugly over the center of the cornea without the need for a fluid space, and the corneal surface of the lens is flatter than the corneal curvature. Unfortunately, with large buphthalmic eyes, direct lens-corneal contact causes distortion of the corneal surface and, again, results in distorted view of the angle. The Swann lens has the advantage of being small enough to permit insertion of the gonioscopy knife at the limbus without obstructing the lens.

Of these lenses, the most widely used for goniotomy is the Worst lens.

Goniotomy Knives

With the lens in position, the next step is to select a suitable goniotomy knife. The most popular is the Barraquer goniotomy knife, which fulfills all the major criteria for a good goniotomy knife:

1) The blade should not be too wide, not exceeding a width of 1.5mm, to prevent leakage along the paracentesis incision.

2) The widest portion of the shaft should equal but not exceed the width of the blade, so that, when the shaft is fully inserted into the eye, it will fill the paracentesis opening and prevent loss of fluid and collapse of the anterior chamber. The shaft of the blade needs to be slightly longer than the diameter of the anterior chamber.

3) A fine metal cannula is attached to the handle and shaft and via a PVC tube to a reservoir filled with balanced salt solution. Balanced salt solution is infused during the operation to maintain a deep anterior chamber. Alternatively, Healon or some other viscoelastic material can be used to maintain the anterior chamber. However, residual Healon may cause a post-operative rise in intraocular pressure and a more severe post-operative iritis.

4) The blade of the knife should be triangular and sharp on both sides to allow it to cut right and left without having to rotate it inside the anterior chamber. (Fig. 15)

Technique

Pre-treatment with topical pilocarpine is useful to constrict the pupil but may shallow the anterior chamber, making the procedure more hazardous.

A goniotomy lens and goniotomy knife are selected, and the knife connected via a PVC tube to balanced salt solution or in a 5cc syringe or I.V. infusion bottle. All air bubbles are removed from the system. The bottle is hung approximately 100-150cm above the eye, and the knife is checked for a suitable rate of infusion, adjusted by the height of the bottle or the force with which the syringe plunger is depressed. The knife is inserted into the anterior chamber through the cornea immediately anterior to the limbus, and under direct visualization and in the presence of a deep AC the knife is advanced across the AC parallel to the plane of the iris and lens surface until it reaches the trabecular meshwork in the area of the angle opposite to the point of insertion. The knife is then farther advanced until the point enters the trabecular meshwork and is then swung to the left and right, incising an area of approximately one-third the circumference of the angle. (Fig. 15) The incision should be into the trabecular meshwork just anterior to the insertion of the iris. As the knife incises the trabecular meshwork, the iris falls backward, and the angle deepens (Fig. 15 showing a Barraquer knife incising the trabecular meshwork). Great care should be taken to avoid incarcerating the



Fig. 15: Barkan Goniotomy Technique

As shown in the inset, the surgeon sits to the temporal side of the patient's head which is turned 30 degrees away from the surgeon. A Barkan goniolens (L) is placed on the eye. The surgeon views the trabeculum with 2x to 4.5x magnification loupes. An assistant provides illumination of the surgical field by aligning a light source such as a hand-held illuminator or fiberoptic (F) along the surgeon's visual axis (dotted arrow). Illumination can also be provided by a focused head light source such as that of and indirect ophthalmoscope (not shown) in which the optical portion has been removed or elevated out of the surgeon's line of gaze. The operating microscope, however, suitably tilted is the best source of illumination and magnification. The goniotomy knife (K) enters the cornea at a point that bisects the arc of the planned 120 degree surgical incision (arrow). While viewing through the goniolens (L), the incision (G) is made sightly anterior to the middle of the trabecular meshwork.

iris in the knife edge or damaging the lens. If the iris is incarcerated, the knife should be withdrawn and then replaced. If bleeding occurs, the rate of fluid infusion into the anterior chamber should be increased to clear the blood and tamponnade the bleeding vessel. If the saline infusion leaks from the AC too rapidly and fails to tamponnade the bleeder, a large air bubble may be introduced to stop the bleeding. At the completion of the incision, the AC will deepen, the knife is carefully withdrawn from the eye, taking care to avoid injury to the iris or lens, and the AC is filled with balanced salt solution and the goniotomy lens removed from the eye.

A drop of an antibiotic/corticosteroid preparation is instilled into the conjunctival sac, and a patch and shield are applied to the eye. The day following surgery, the AC should be deep and the pupil reactive. Topical antibiotic/corticosteroid drops are continued until the AC reaction resolves.

Surgical Technique for Trabeculectomy/Trabeculotomy

The technique for trabeculectomy is described in detail in another chapter, and only an outline of the surgical technique is offered here.

Conjunctival Flap (5x magnification)

A 7mm fornix-based conjunctival flap is raised in the superior conjunctiva and reflected back to expose sclera, with sufficient space to produce a 3mmx3mm lamellar scleral flap. A one-third-thickness scleral flap hinged at the limbus is raised and rotated anteriorly onto the cornea. The external surgical landmarks, as previously described, are now visible (i.e., deep corneal tissue anteriorly, a band of trabecular meshwork tissue behind it, and sclera posterior to the trabecular meshwork bands).

A 2mmx2mm block of scleral tissue is outlined in the deep corneal and trabecular meshwork tissue, the base of the scleral flap extending posteriorly to the scleral spur. This block is incised to the deep layers without entering the AC.

A radial incision is cut across the trabecular band and across the scleral spur as previously described for trabeculotomy and dissected until Schlemm's canal is identified. The outer wall of Schlemm's canal is dissected into its lumen, and approximately 1.5mm of outer wall is removed using Vannas scissors, as previously described (sinusotomy). At the completion of the trabeculotomy, the anterior chamber should remain intact. Attention is now directed to the 2mm x 2mm square of corneal and trabecular tissue previously outlined, and the tissue is excised, as described for trabeculectomy in Chapter 18.

An alternative technique for exposing Schlemm’s canal is by deep sclerectomy as described in Chapters 22 and 26.

This procedure is used for those patients in whom one or more trabeculotomies have failed, and for those children in which the developmental angle anomaly falls into the group of cicatricial angle anomalies or iridocorneal dysgenesis.

Other Surgical Procedures for CIJ Glaucoma

Plastic Drainage Devices

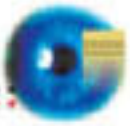
These devices are reserved for those eyes refractory to all treatment, including trabeculotomy and combined trabeculotomy/trabeculectomy. When these procedures have failed, there are a number of drainage devices available.

1. Simple setons placed through the sclera just posterior to the limbus and extending into the AC. These are universally unsuccessful in the long term.

2. Krupin-Denver valve prosthesis, manufactured by Storz, is a plastic seton with a pressure-sensitive valve at the end of the tube which controls the flow of aqueous through the seton. In the author's experience, this prosthesis has not been highly successful.

3. The Molteno seton has been used for over 20 years with good results in congenital glaucoma. However. it has the disadvantage of not having a valve, so that post-operative hypotony may be a problem.

4. The Baerveldt seton is popular but has the same disadvantage as the Molteno.



5. The Ahmed valve prosthesis is a long-tube seton with a large base plate and a valve situated in the base plate. This prosthesis has worked well in the author's hands and is the procedure of choice, as the valve will prevent postoperative hypotony in most cases.

These setons and the surgical technique for implanting them are described in detail in a subsequent chapter.

Ciliodestructive Surgery

These procedures, in particular, Nd:YAG cyclophotoablation or diode laser cyclophotoablation, are used as a last-ditch procedure if all other surgical procedures have failed. They may be successful in reducing intraocular pressure, but generally only for a limited time. The surgical method is described in detail in Chapter 42.

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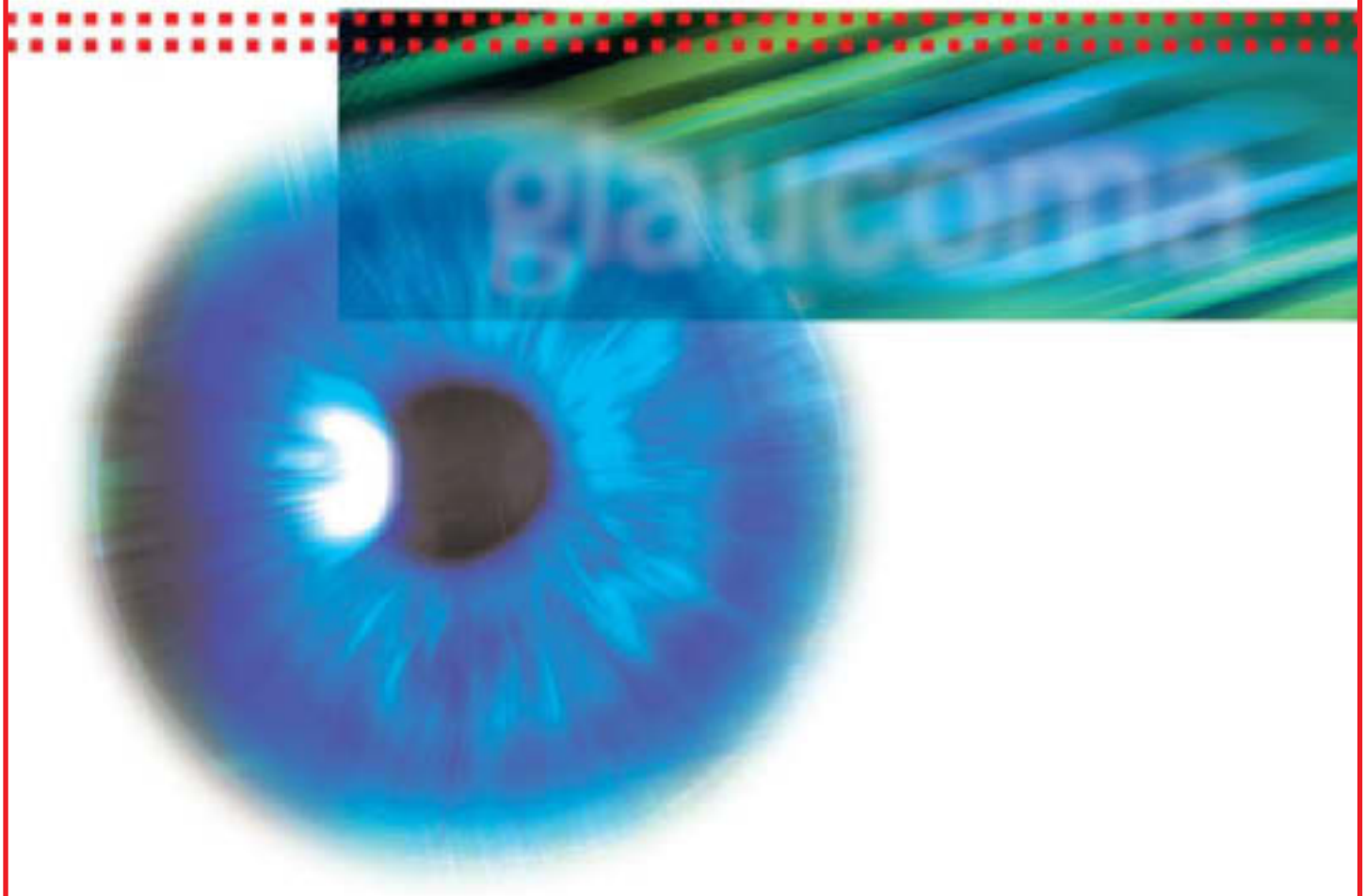


SECTION IV

Surgical Management of Primary Open Angle Glaucoma

- The Laser Trabeculoplasties and Sclerostomies
- Incisional Surgical Management
 - A. Trabeculectomy
 - B. The Non-Penetrating Filtering Operations

The Laser Trabeculoplasties and Sclerostomies



Chapter 15
ARGON LASER TRABECULOPLASTY

Benjamin F. Boyd, M.D., F.A.C.S.
Maurice Luntz, M.D., F.A.C.S.

The Role of ALT - Indications

Although some ophthalmic surgeons do not believe much in its efficacy, argon laser trabeculoplasty first introduced by Jim Wise[1] is still considered as a useful adjunct to medical therapy in primary open angle glaucoma. In a sense, it acts as a valuable added medication.

Stamper[2] considers that laser trabeculoplasty is still the treatment that one uses between the failure of well tolerated medical therapy and incisional surgical therapy. If it fails, filtering surgery is usually advised. Paul Lichter, M.D., points up that sometimes, when the physician believes that intraocular pressure must be reduced to as low a level as possible, argon laser trabeculoplasty is not used at all.[3]) Instead, filtration surgery is undertaken instead of laser trabeculoplasty.

Nagasubramanian points up that in the strictly controlled studies made at Moorfields Eye Hospital in London, comparing medical therapy vs argon laser trabeculoplasty (ALT) vs trabeculectomy as initial, primary therapy, in the majority of patients treated with laser, for the first year or two the pressure remains controlled but subsequently, a significant number of these patients tend to drift and the pressure is no longer maintained as it was.[4] After two years, many of these patients needed additional medical therapy and a few required surgical intervention because of the unacceptable level of pressure.

Richard Simmons, M.D., who was one of the pioneers of ALT and has extensive experience with the procedure, considers that it is a useful technique, that it can have a decrease in its effect with time but many procedures lose effect with time and still can be very valuable.[5] This does not prevent him from using it effectively. However even if patients benefit for a year or two and up to five years and delay surgery, this is a great benefit. In some patients its beneficial effect can last a lifetime.

Re-treatment is possible. About a third of the cases can respond to re-treatment. It should be tried in patients where the initial ALT has been helpful, not when it was not initially useful.

Argon laser trabeculoplasty is considered safe and effective in lowering intraocular pressure. In some cases, it is appropriate to use it as initial therapy. These cases are: 1) in patients who cannot or will not comply with prescribed medical therapy. 2) in certain parts of the world where adequate medical treatment is not feasible because of socio-economic limitations.

A recent major study concludes that ALT as an initial treatment for open angle glaucoma is as safe and as effective as medical treatment. ALT is an acceptable option to medical treatment as the initial treatment for open angle glaucoma. (See Chapter 9).

ALT, however, is not widely used as initial therapy because its IOP lowering effect is limited to on average 2 1/2 years. When the full effect of ALT is lost the patient then has to use medications.

Furthermore, in many patients ALT does not adequately control the IOP and the patient still requires medication.

In all cases, to be successful, the angle does have to be open, the media must be clear and one must have access to the trabecular meshwork. **James B. Wise, M.D.**, who developed ALT, has observed that population groups of phakic patients do better than aphakic. It appears that aphakia does interfere with response to the laser, probably by the influence of vitreous in the anterior chamber and the trabecular meshwork. Interestingly enough, pseudophakic patients respond to the laser very similarly than phakic patients. That is, the presence of the posterior chamber lens implant keeping the vitreous out of the anterior chamber greatly improves the response to the laser. Eyes with anterior chamber lenses and glaucoma usually show a poor laser response, due to uveitis and trabecular damage from the lens.

The older the patient is, the better the results. Pressure reduction with ALT is not the same in patients of different races. In Mexico, for instance, where the majority of patients are descendants from the Aztec and Mayan "indian" races, the results with ALT are very poor. As a consequence, ALT is rarely done in that country. African and Caribbean black patients do not respond as favorably as white Caucasian patients.

ALT and Medical Therapy - Complementary Methods

Hugh Beckman,[5] coordinated the Glaucoma Laser - Trial Research Group reported recently, in which patients with newly diagnosed primary open angle glaucoma were randomly assigned to either ALT as the first treatment or beta-blockers as the first treatment. Beckman points out that neither laser alone nor medication alone represents "a magic bullet". If he is certain the patient has primary open angle glaucoma, he offers the patient ALT first. If he is not sure of the diagnosis, he starts with medication. Medical therapy is reversible, but laser therapy is not. (See Chapter 9).

From the evidence at hand, it is quite clear that the combined use of beta-blockers and ALT is a highly effective method of controlling open angle glaucoma, certainly better than either method alone. They are complementary methods of treatment.

Mechanism of ALT

The cellularity of the normal human trabecular meshwork is reduced as a consequence of aging. The glaucomatous eye also shows a loss of trabecular cells compared with the normal eye and a trabecular relaxation which interferes with drainage.

Beckman[5] points out that the accepted concept on how laser trabeculoplasty reduces intraocular pressure is that it causes a small amount of shrinkage in the areas adjacent to the trabecular meshwork and segmental shrinkage to the canal of Schlemm. As a result, the trabecular structures stretch, and thus the intra trabecular spaces and the collector channels enlarge (Fig. 1).



Fig. 1: **Conceptual View of Mechanism of Argon Laser Trabeculoplasty**

Above, the mechanism of LTP is depicted in a more detailed close-up view of the angle area. (A) Shows the loss of trabecular cells in a glaucomatous eye and a trabecular relaxation (T-1) which interferes with drainage. In Fig. B, laser applications (L) placed on the margin of the anterior pigmented band will provoke a small amount of shrinkage in the areas adjacent to the trabecular meshwork and segmented shrinkage to the canal of Schlemm. As a result, the trabecular structures stretch and thus the intra-trabecular spaces and the collector channels enlarge.

Technique of Argon Laser Trabeculoplasty (ALT)

The Role of Apraclonidine - One vs Two Stages

Apraclonidine has become the accepted prophylactic treatment to prevent pressure rises following laser surgery in glaucoma, or following posterior capsulotomy. Usually one drop is applied one half to one hour before and one drop immediately after the laser treatment. This medication, in this dosage, will prevent a serious pressure rise from occurring in the vast majority of the cases, although it is not always effective.

If apraclonidine is not used, ALT performed 360º at one sitting can be followed by a very significant pressure rise, sometimes into the 40's, 50's, even 60's, which can cause further damage to the optic nerve or even wipe out a very contracted visual field.

Aprachlonidine is no longer freely available. One drop of Trusopt 2% (Dorzolamide) is also an effective prophylactic treatment when given prior to ALT using Trusopt 2%. Most glaucoma experts are moving back to performing 360 degrees of ALT at one sitting instead of doing 180 degrees at a time. Apraclonidine is no longer freely available.

The Choice of Laser Used

The traditional laser used for years in this technique is the argon laser, with blue or blue-green light. Recent trials published by Brancato in 1991 show that the ALT with diode laser using green light is just as effective in reducing intraocular pressure as compared with the argon green ALT. The main difference is that with diode ALT the visualization of the spots on the trabecular meshwork is quite difficult. Brancato has shown, however, that diode ALT can be considered safe and effective as well as argon ALT.[6]

Applying the Laser Beam in the Right Place

The laser beam is applied to the surface of the trabeculum meshwork through a coated mirrored Goldmann goniolens through the clear cornea. When performing a 360º ALT at one sitting, about 100 burns are placed in the angle all the way around the circumference of the eye, about 3.6 degrees apart, through the goniolens utilizing a very finely focused beam of argon laser energy. This is applied to the posterior trabecular meshwork, the most functional part of the trabecular meshwork (Fig. 2). By this we refer to the portion of the trabecular meshwork just anterior to the scleral spur. If one were to divide the space between the scleral spur and Schwalbe's line in half, the burns would be placed in the center of the posterior half (Fig. 2). That is, centered on the posterior trabecular meshwork or filtration portion of the meshwork. This area appears as a pigmented band in the pigmented trabecular meshwork and as a grayish band anterior to the scleral spur in an unpigmented eye. The anterior trabecular meshwork would be left untreated.

Clinically there are two zones to the trabecular meshwork: a zone which consists of about half of the width of the meshwork and is just in front of the scleral spur, and another zone which consists of about half of the width of the trabecular meshwork, which is adjacent and just posterior to Schwalbe's line (Fig. 2).

In the pigmented eye the posterior trabecular meshwork has pigment in it; it is a pigmented band. In the unpigmented eye it is of different consistency and grayish. In the eye that has blood in Schlemm's canal one can see that it directly overlies Schlemm's canal. It provides, therefore, a distinct target in the angle for which one can aim. That is what we refer to, clinically, as the posterior meshwork. This is not a histologic term. It is a term which is convenient in clinical usage. Others may refer to it as "the filtration

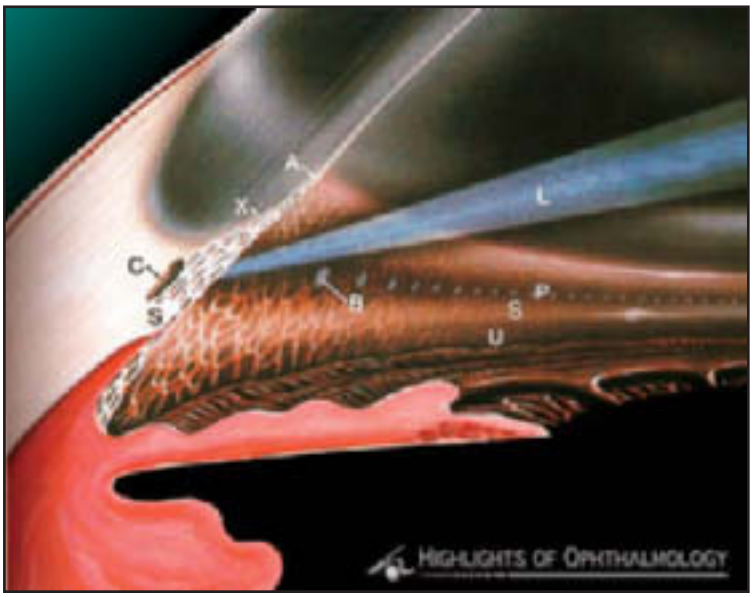


Fig. 2: Proper Placement of Laser Application in Laser Trabeculoplasty

This magnified cross section of the angle area shows a properly placed laser beam (L) being applied to the center of the posterior trabecular meshwork (P) or pigmented band. Notice the laser burns (B) centered on this pigmented band (P). If one were to divide the space between the scleral spur (S) and Schwalbe's line (A) in half (X), the laser burns (B) fall on the center of the posterior half (area between (X) and (S)). The anterior half of the meshwork (area between (X) and (A)) is left untreated. Posterior to the scleral spur (S) is the uveal meshwork (U). Schlemm's canal (C).

portion of the meshwork" or "the portion of the trabecular meshwork that overlies Schlemm's canal".

Most surgeons place the argon laser burns at the anterior border of the area that we have described clinically as the posterior trabecular meshwork. There is universal agreement that the area anterior to Schwalbe's line should not be treated. Most surgeons prefer to treat anterior to the scleral spur because most believe you may get more exudate, fibrin and synechiae formation if you treat posteriorly. Consequently, most surgeons apply laser therapy in the region between the scleral spur and Schwalbe's line (Fig. 2).

Attainment of Proper Size of Laser Burn

Jim Wise, M.D.,[1] has emphasized that by far the most important variable in ALT is the spot size produced by the laser. It is important to apply a true 50 micron spot size (Figs. 3,4,5).

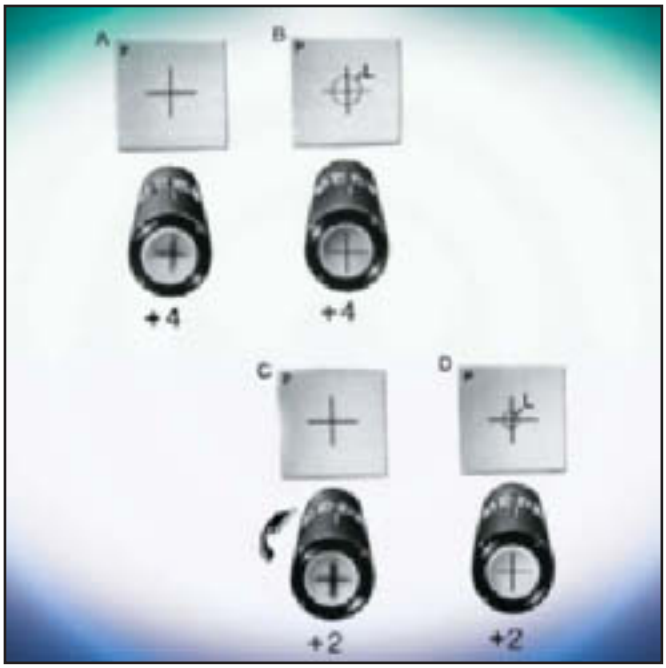


Fig. 3: Procedure for Attaining Proper Size of Laser Burn

First, the laser is set to a 50 micron spot size. In (A), a piece of paper (P) is taped to the slit-lamp headrest. The + on this paper is added here as a focusing target for illustration purposes only. The eyepiece setting is placed on +4 as shown. Then the paper is brought into focus by use of the joystick. In (B), the paper is in focus (i.e., the + is clear in the eyepiece). With the setting still on +4, a laser burn (L) is made on the paper (P). The burn spot size is measured and as an example, it is found to be 100 microns and too large. This means that the 50 micron size aerial point of focus of the laser beam is not on the paper even though the eyepiece is focused on the paper, at this eyepiece setting of +4. Additional eyepiece settings are tried following this same routine. Example (C) shows a +2 eyepiece setting (arrow) and the paper focused in as before. In (D), the paper is in focus (clear + image seen through the eyepiece), the laser burn (L) is measured and found to be 50 microns in diameter on the paper (P). Thus, with this laser, a +2 eyepiece setting should be used in all treatments. In this case, with a +2 eyepiece setting and the trabeculum in focus, the aerial point of focus of the 50 micron laser spot will be on the trabecular surface.

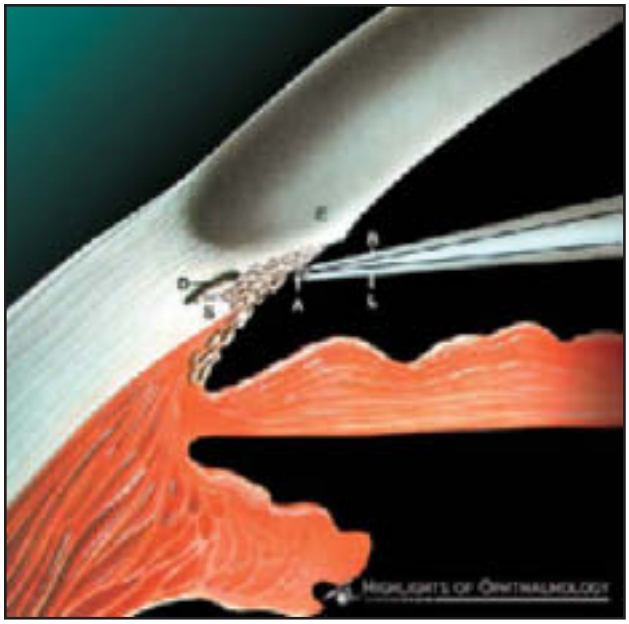


Fig. 4: Attainment of Proper Size of Laser Burn

This magnified section of trabeculum shows the "aerial point of focus" (the 50 micron size circle at (A)) of the laser beam (L) and the viewer's eyepiece focal point (solid lines (B)) both converging at the same point on the trabeculum. This results in a proper 50 micron burn size on the trabeculum with a simultaneous clear, focused view of the trabeculum through the eyepieces. Cornea (E). Schlemm's canal (D). Scleral spur (S). To properly adjust the laser in this manner, see Fig. 3.

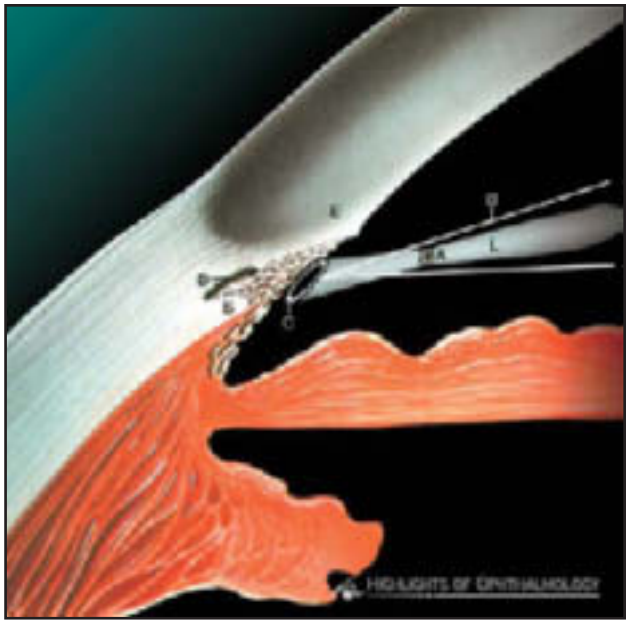


Fig. 5: Principal Cause of Improper Laser Burn Size

This magnified view of the anterior trabeculum shows the major reason for oversize laser applications. Shown above, the surgeon sees the trabeculum clearly in focus (depicted by solid lines (B) which come to a focused point on the trabeculum) but the point of focus (A) of the laser beam (L) is in front of the trabeculum. Adjusted as such, the laser beam diverges beyond this "aerial point of focus" (A) to create an improper, larger than 50 micron spot size (larger circle at (C)) on the trabeculum. The goal is to adjust the viewing eyepieces so that they focus at the same location (on the trabeculum) as the laser beam 50 micron focal point, as shown in Fig. 4. Then, when the surgeon focuses the eyepieces on the trabeculum, the 50 micron laser spot will fall on the trabeculum. Cornea (E). Schlemm's canal (D). Scleral spur (S).

Unless you know how to make this adjustment (Fig. 3) you will be using large spots. (**Editor's Note**: for attainment of proper size vs improper size of laser burn, see Figs. 4 and 5). Also many lasers are not properly adjusted by the manufacturer and cannot give a 50 micron spot at any eyepiece setting.

The mathematics of oversized spots are frightening. If, for example, a physician by error is using a 100 micron spot rather than a 50 micron stop, and this is easy to do, then 100 of his/her laser spots are equivalent to 400 of the 50 micron laser spots and will be grossly overtreating the patient. Wise is certain that the majority of bad results reported are due to lack of ability to deliver a true 50 micron spot to the trabecular meshwork.

Technique for ALT

The patient is placed at the slit lamp, ensuring that the patient is comfortable in the headrest. Prior to placing the patient at the slit lamp, one drop of apraclonidine or dorzolamide is placed in the eye to be lasered about one half-hour before laser surgery. Once the eye is anesthetized, just prior to laser surgery, using topical anesthesia, a 2- or 3-mirror Goldmann goniolens filled with Goniosol or methylcellulose is placed in the eye to be lasered in order to give the surgeon a clear view of the angle. The laser is set at the 50-micron aperture, 0.1 sec. duration and 1.10 W power (Fig. 6). The inferior angle is visualized, as laser burns are generally placed first in

the inferior angle because it is the widest part of the anterior chamber angle. The laser spot is placed anterior to the scleral spur in the posterior or anterior trabecular meshwork but posterior to Schwalbe's line. The laser is activated, and the first laser burn is made. If a gas bubble forms in this burn, the laser power is reduced. If there is no gas bubble, the laser power can be increased, in either case by about 10mW. The ideal calibration in each particular patient is a burn that is just below the level at which a gas bubble forms. Once this calibration is reached, the burns are placed in the same layer of the angle, placing burns adjacent to the one another to achieve 25 burns per quadrant. Either 50 burns over 180º are placed, or 100 burns over 360º.

ALT in Combined Mechanism Glaucoma

Combined mechanism glaucoma refers to the presence of open angle glaucoma plus a component of angle closure glaucoma without extensive closure. This type of glaucoma is a problem to manage but it can be successfully treated with the argon laser. If there is significant closure in the angle, at first a laser iridectomy must be performed (See Chapter 28 on Primary Angle Closure Glaucoma). It is preferable to do this in a separate session rather than combine it with laser trabeculoplasty. Therefore, after eliminating the angle closure with the laser iridectomy, we can use laser trabeculoplasty at a separate session. This is an effective combination. To do both at one sitting is possible but, because of the extra degree of inflammation created, it is preferable to perform them separately. Also, gonioplasty, the application of laser to the peripheral iris in order to pull the iris taut and away from the trabecular meshwork, can be tried on areas of angle with near closure to possibly allow better access of the laser beam to the trabecular meshwork when treating with trabeculoplasty. (See Section V on Primary Angle Closure Glaucoma).

Complications of ALT

The complications are: iritis, hemorrhage from the trabecular meshwork during treatment

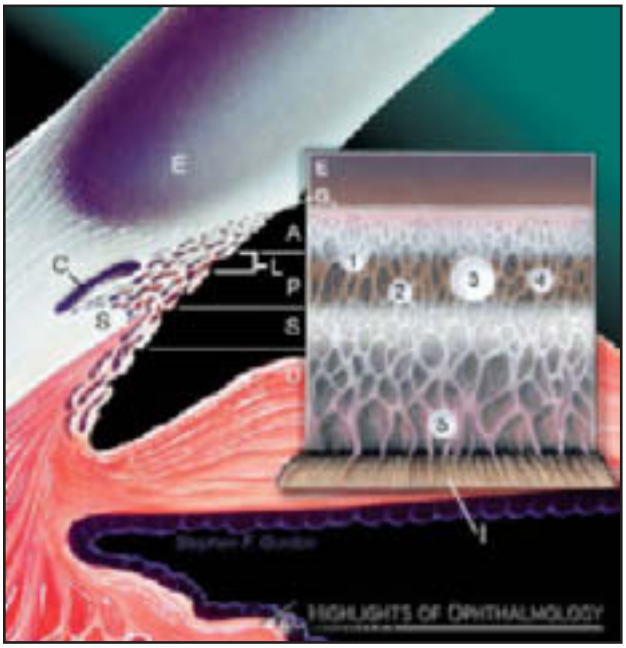


Fig. 6: Applying Laser Burns Correctly in ALT

Cross-section to the left; Cornea (E), Schlemm's canal (C), scleral spur (S), Schwalbe's line (G), anterior corneoscleral meshwork (A), pigmented band (P) and uveal meshwork (U). Proper placement of the 50 micron laser burn (L) is shown at the anterior margin of the pigmented band (P). To the right, gonioscopic view with iris (I) below. Properly placed 50 micron laser burn at the anterior pigment band (P) shown at (1). A misplaced burn is shown at (2) along the posterior margin of the pigment band (P). An oversized burn is shown at (3), spanning the entire pigment band. A slightly misplaced burn is shown at (4) in the middle of the pigment band. A seriously misplaced burn into the uveal meshwork (5).

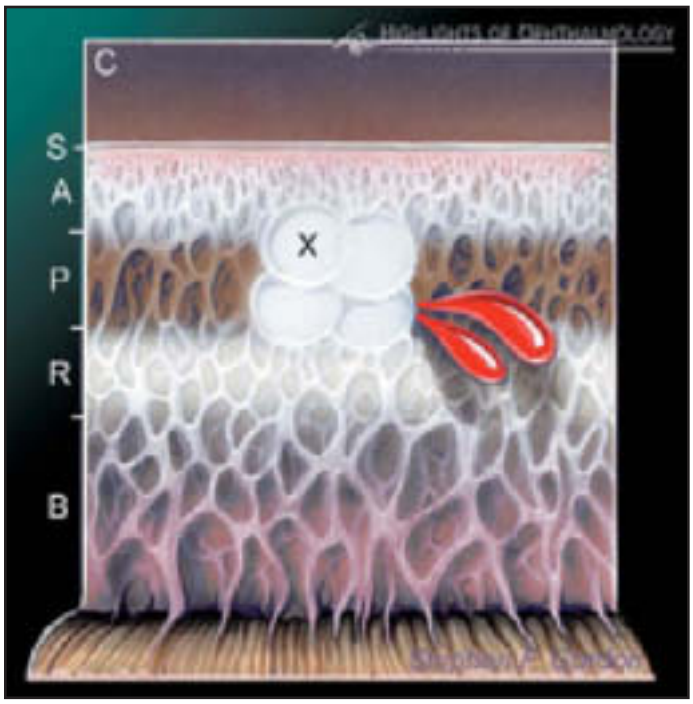


Fig. 7 Use of Laser to Stop Hemorrhage in ALT

In the trabeculum above, the bleeding has been stopped by placement of a few large size-low power burns (X) to the area.

(Fig. 7) the formation of peripheral anterior synechiae and an elevation of intraocular pressure following ALT.

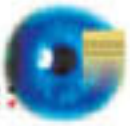
In most cases the iritis is transient, mild and easily controlled with topical steroids for a few days. In many eyes the iritis will resolve spontaneously and you do not need topical steroids. In a few cases hemorrhage from the trabecular meshwork may be encountered during treatment (Fig. 7). There are two patterns of hemorrhages that can occur. The most frequent one is where the hemorrhage occurs all of a sudden apparently arising from the point of application of the laser beam. The other pattern is a slow oozing of blood through the meshwork stemming from areas of untreated meshwork just adjacent to the sites of laser application.

You may attempt to control the bleeding by applying moderate pressure on the globe with the Goldmann contact lens. As one observes the bleeder through the mirror in the slit-lamp, if it has not stopped after applying gentle pressure to the globe, one can try the opposite, that is, actually withdraw the lens creating a suction effect. This also reduces the pressure of the Goldmann lens on the episcleral veins. In some cases the bleeding is induced by the contact lens raising episcleral venous pressure. Therefore, by reducing this in some cases the bleeders stop as we release the pressure on the episcleral veins.

If these techniques fail, you may apply a few laser burns of relatively large spot size and low power to the point of bleeding on the meshwork (Fig. 7).

Peripheral anterior synechiae occur in about half of cases treated. These may develop from several weeks to several months after laser trabeculoplasty. In most of these eyes the synechiae extend to the level of the scleral spur or ciliary body and, in a minority of eyes, they extend to the trabecular meshwork. No long-term deleterious effects on facility of outflow or pressure reduction have been found from the PAS (peripheral anterior synechiae).

The major complication is an elevation of intraocular pressure after treatment, ranging from 1mm to 25mm above baseline. This occurs in about 25% of all eyes treated but can be prevented by instilling Apraclonidine or dorzolamide before and after ALT as previously discussed.



Mark Latina, M.D., has devised a new approach to standard ALT in which pigmented trabecular meshwork cells are selectively targeted. (See Section on "Selective Laser Trabeculoplasty").

Medical Therapy Following ALT

It is very important that the same adequately tolerated glaucoma medical therapy that the patient was using preoperatively be continued. If one stops it, there is danger of pressure rise and lack of control of the glaucoma. In addition, this therapy is supplemented with anti-inflammatory topical steroids, such as Prednisolone acetate 1% every hour for the first two days and then q.i.d. during the first week following ALT.

After two months or so, the question arises whether medications could be tapered or not. We should not be eager to stop well tolerated medical therapy because the group of patients that we are dealing with usually have damaged discs and fields. We certainly can taper and reduce in some cases medications that are poorly tolerated or have borderline intolerance. Any important decrease in medical therapy should be done cautiously, one medication at a time, with frequent monitoring of the intraocular pressure.

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Chapter 16
SELECTIVE LASER TRABECULOPLASTY

Mark A. Latina, M.D.
Joseph Anthony Tumbocon, M.D.

Concept

Argon laser trabeculoplasty was first described by Wise & Witter[1] in 1979 and has been viewed as an alternative to surgery in patients whose open angle glaucoma (OAG) could not be adequately controlled by medications. This treatment modality has been gaining popularity as an effective treatment option in patients with OAG as shown in the Glaucoma Laser Trial and Glaucoma Laser Trial Follow-up Study.[2] The investigators demonstrated that eyes treated initially with argon laser trabeculoplasty had lower intraocular pressures and better visual field and optic disk status than their fellow eyes treated initially with topical medications.

However, ALT has also been observed to produce some deleterious effects to the microstructure of the trabecular meshwork. Histopathologic studies have shown that argon laser trabeculoplasty results in coagulative destruction of the uveoscleral meshwork in the areas of the laser spots and causes heat-damage to the surrounding structural collagen fibers. Furthermore, a membrane formed by migrating endothelial cells was noted on the meshwork between the applied argon laser spots.[3,4,5,6] This membrane covering meshwork after argon laser trabeculoplasty (ALT) has been postulated to be the cause of late outflow reduction, pressure increase and treatment failure. Additionally, damage to the trabecular meshwork structure caused by ALT theoretically limits future medical and/or repeat laser treatment.

Selective Laser Trabeculoplasty (SLT) represents an improvement over conventional ALT by eliminating thermal damage of trabecular meshwork (TM) architecture. Using a low energy, Q-switched, frequency doubled Nd: YAG Laser emitting at 532 nm with a pulse duration of 3 nanoseconds, Latina, Park and Sibayan[7,8] demonstrated isolated destruction of the pigmented TM cells without producing any thermal nor collateral damage to the

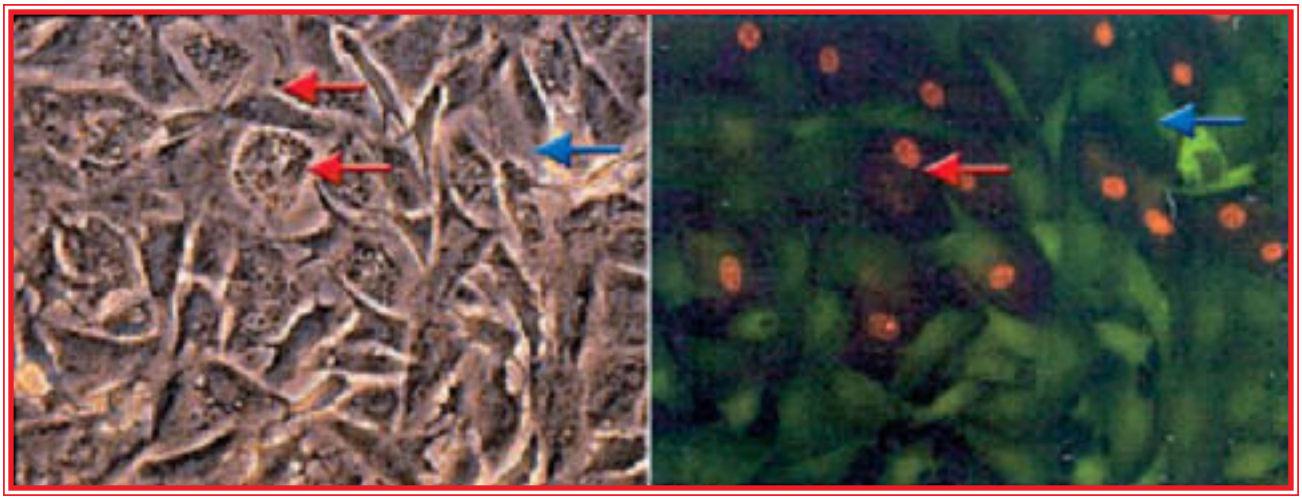


Figure 1. Figure on the Left: Phase contrast micrograph of pigmented & non-pigmented trabecular meshwork (TM) cells. Figure on the Right: Photomicrograph using fluorescent viability/ cytotoxicity assay after irradiation with SLT. Only the pigmented TM cells exhibited nuclear staining (orange fluorescence) and absence of cytoplasmic staining (green fluorescence) which indicate cell death (red arrow). The non-pigmented TM cells were not affected with SLT as shown by the presence of cytoplasmic staining and absence of nuclear staining in these cells (blue arrow) .

surrounding non-pigmented cells and trabecular collagen beams (Figure 1). Furthermore, endothelial membrane formation on the TM, which is usually found in ALT treated eyes, was not observed after SLT exposure in vivo. These histologic findings were confirmed by Kramer and Noecker[9], where they compared the acute morphologic changes in the TM of human eye bank eyes after ALT and SLT by scanning and transmission electron microscopy. After laser irradiation, ALT produced crater formation, coagulative damage, fibrin deposition, disruption of trabecular beams and endothelial cells. SLT did not exhibit the aforementioned findings and the general structure of the TM was preserved. In contrast, the effect of SLT occurred in the intracellular level, wherein disruption of the melanin granules was observed. The lack of thermal and structural damage to the TM makes SLT potentially repeatable.

The in vitro and in vivo findings after SLT are observed because the pulse duration of SLT is much shorter (3 nanoseconds) than the thermal relaxation time of the target chromophore (melanin) in the pigmented TM cells.[7] Thermal relaxation time defines the absolute time required by a chromophore to convert electromagnetic energy in to thermal energy. Melanin has a thermal relaxation time of approximately 1 microsecond, while the pulse duration of the SLT is 3 nanoseconds. This means that the pulse duration of SLT is too short for the melanin to convert the electromagnetic energy to thermal energy and, thus, no heat is liberated. Therefore, this spares the surrounding non-pigmented tissues from any damage.

The IOP reductions observed after SLT provide an additional insight into the potential mechanism of IOP lowering after TM laser treatment. Selective trabeculoplasty is not associated with coagulation damage, yet it significantly lowers the IOP. This indicates that coagulation of the TM structure is not an important component to the mechanism of

IOP lowering after SLT. The demonstrable clinical efficacy suggests that laser trabeculoplasty works on the cellular level, either through migration & phagocytosis of TM debris by the macrophages[10] or by stimulation of formation of healthy trabecular tissue which may enhance the outflow properties of the TM.[11,12] Alvarado[13] has observed a 5 to 8 fold increase in the number of monocytes and macrophages present in the trabecular meshwork of monkey eyes treated with SLT as compared with untreated controls. He theorized that injury to the pigmented TM cells after SLT results in the release of factors and chemo-attractants which recruit monocytes which are activated and transformed into macrophages upon interacting with the injured tissues. These macrophages then engulf and clear the pigment granules from the TM tissues exits the eye to return to the circulation via the Schlemm's canal.[14] All these events have been postulated to play a role in the IOP lowering effect of SLT.

Clinical Studies

In 1998, a pilot clinical study was conducted to evaluate the intraocular pressure lowering effect of Selective Laser Trabeculoplasty in 53 open angle glaucoma patients whose intraocular pressures could not be controlled with maximum medical therapy (Max Rx group) or had a previous failed argon laser trabeculoplasty (PFLT group).[15] Seventy per cent of the patients responded with an IOP reduction of at least 3 mmHg. At 26 weeks of follow up, the mean IOP reduction was 23.5% ($p<0.001$) for the Max Rx group, 24.2% ($p<0.001$) for the PFLT group, and 23.8% ($p<0.001$) for both groups combined (Figure 3). The promising results of this study led the investigators to embark on a prospective, multicenter clinical trial which involved 101 eyes of 101 patients in four clinical sites (Advanced Glaucoma Specialists, Reading MA; New York Eye and Ear Infirmary, New York, NY; University of Arizona Health Sciences Center, Tucson, AZ; Kresge Eye Institute, Detroit, MI).16 Forty five eyes were on maximum tolerated medications (Max Rx group) and 56 eyes had a previous failed argon laser trabeculoplasty (PFLT group). Thirty four of the 45 patients (75.6%) in the Max Rx group, 37 of the 56 patients (66.1%) in the PFLT group responded to treatment with an IOP reduction of at least 3 mmHg up to the 26th week post-SLT. The mean IOP reduction was 5.2 mmHg (20.3%, $P<0.0001$) for the Max Rx group, 3.8 mmHg (14.7 %; $P< 0.001$) for the PFLT group, and 4.4 mmHg (17.2%, $P<0.001$) for both groups combined. (Figure 2) The mean number of glaucoma medications decreased from baseline by 1.2 medica-

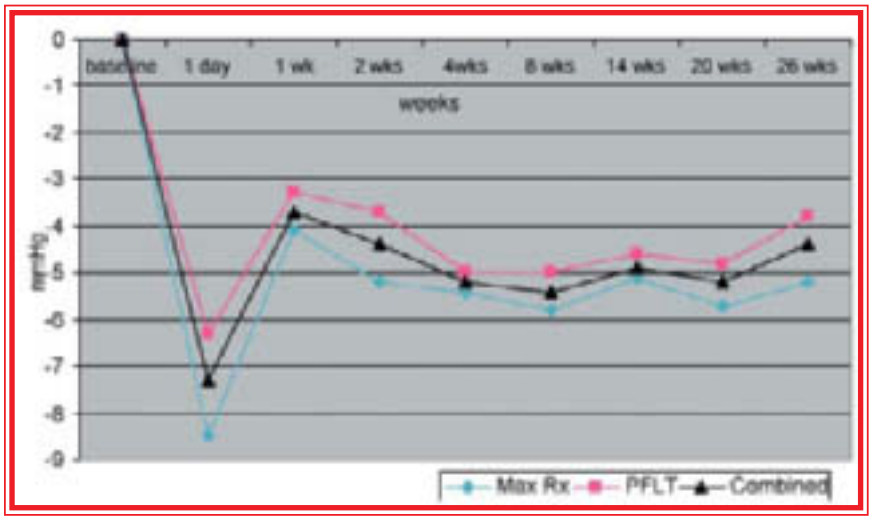


Figure 2. Mean Reduction of Intraocular Pressure in 101 SLT Treated Eyes16 (Max Rx – OAG uncontrolled by maximum medical therapy; PFLT – uncontrolled OAG with a previous history of ALT treatment; Combined – all SLT treated patients in the study).

tions. Mild anterior chamber reaction commonly occurred within after SLT irradiation, which usually decreased within 24 hours and was completely resolved by 1 week. The adverse events observed were minimal, transient and were similar to that seen after ALT treatment. An IOP elevation of > 10 mmHg above the immediate preoperative IOP was observed in 7 (5.8%) of the treated eyes. Elevated IOP occurred within 1 to 24 hours after treatment in 5 patients and between 1 to 7 days in the other two patients. (the patients did not receive any prophylactic medications against postoperative IOP spikes). The IOP elevations were managed with topical anti-glaucoma medications and usually resolved within 24 hours. Six patients (5%) experienced eye pain, while another group of 6 patients (5%) developed non-specific conjunctivitis after laser treatment. Other adverse events occurring at less than 1% incidence were blurred vision (0.8%), corneal edema (0.8%), and appearance of a corneal lesion (0.8%) . It should also be stressed that no peripheral anterior synechiae developed in any of the eyes treated with SLT.

What is noteworthy in both studies was that more than 66% of the patients who had a previous failed argon laser trabeculoplasty (PFLT group) had an IOP decrease of 3 mmHg or greater after treatment with SLT. This figure is much higher than those found in literature in which a failed ALT was retreated with another course of ALT where only 32% had an IOP decrease of 3 mmHg or more.[17] This observation was also supported by the findings of Damji & co-workers[10], where they observed that in patients who had a previous history of failed ALT, a significantly greater mean IOP reduction was observed with SLT (6.8 mmHg) as compared to the patients whose eyes were re-treated with another session of ALT (3.6 mmHg).

Investigators in other countries have also demonstrated the safety and efficacy of SLT in lowering the intraocular pressure. (Table 1) Kaulen[18] in Germany observed that SLT decreased the mean IOP by 23% in 460 eyes of 328 patients, and the procedure had a 2 year success rate of 80%. The complication rate for SLT in this study was approximately 4.5%, which is much lower than the compli-

	Latina et al.[8] 1998	**Kaulen[18] 2000**	**Latina et al.[16] 2001**	**Hong et al.[19] 1998**	**Damji et al.[10] 1999**
Type of study	Prospective, Clinical	Prospective Clinical	Prospective, Clinical	Randomized, prospective	Randomized, prospective
No. of eyes treated	53 eyes	460 eyes	101 eyes	45 eyes	36 eyes
Duration of follow up	6 _ months	24 months	6 _ months	6 months	6 months
Mean IOP decrease after **SLT**	23.8%	23%	17.2%	30.5%	21.9%
Mean IOP decrease after **ALT**				18.5%	21.3%

Table 1. Mean intraocular pressure reduction after Selective Laser Trabeculoplasty (SLT)

cation rate of ALT (which may reach up to 34%2). The most common complications noted were: (1) elevation of IOP in 11 eyes (2.4%) post-operatively (2) significant inflammatory reaction in the anterior chamber without an IOP spike in 7 eyes (1.5%). All the complications were easily treatable with the appropriate eye medications (e.g. steroids).

Damji et al.[10] in Canada embarked on a prospective randomized clinical trial comparing the effectiveness of SLT and ALT in lowering intraocular pressure in 36 eyes. The IOP lowering effect of both treatment modalities at 6 months were observed to be equivalent ($p = 0.97$), with SLT and ALT lowering IOP by 4.8 mmHg (21.9%) and 4.7 mmHg (21.3%), respectively. Likewise, in a similar study involving 45 Asian eyes, SLT and ALT was noted to have an IOP lowering effect of 30.5% (6.3 mmHg) and 18.5% (3.7 mmHg), respectively.[19]

Method

The procedure is performed similar to a conventional ALT. Pre-operatively, careful gonioscopy should be done to carefully visualize the trabecular meshwork (TM) and plan the treatment area.

Laser and Delivery System

The procedure is done with the Coherent Selecta 7000 Frequency Doubled, Q-Switched, Nd:YAG Ophthalmic Laser (Coherent, Inc, Palo Alto, CA)(Figure 3) which delivers 532 nm wavelength of laser light at pulse duration of 3 nanoseconds with a spot size of 400 um. This laser is specifically designed for this procedure. Nd:YAG , argon, diode, and CW frequency doubled Nd:YAG lasers



Figure 3. Coherent Selecta 7000 Frequency Doubled Nd:YAG Ophthalmic Laser (Coherent, Inc, Palo Alto, CA)

cannot be used for this procedure since their pulse duration is longer (microsecond range) and will not produce the same effects as SLT.

Laser Treatment of the Trabecular Meshwork

Pre-operative medications consist of a drop each of Iopidine or Alphagan and topical anesthesia (e.g. Proparacaine). A Goldman three-mirror goniolens is then placed on the eye with methylcellulose. The aiming beam is then focused onto the pigmented trabecular meshwork (TM). The 400 um spot size is large enough to irradiate the entire anteroposterior height of the TM (Figure 4).

The visible endpoints of typical of conventional argon laser trabeculoplasty, such as blanching of the TM or bubble formation within the TM, are not seen with SLT. To determine the optimum energy level for Selective Laser Trabeculoplasty for each eye, the Nd:YAG laser energy is initially set at 0.8 mJ, and then the energy level was increased by 0.1 mJ until the threshold energy for bubble formation is observed. After the threshold energy was identified or if bubble formation is already noted at the initial energy level, the laser energy level is decreased by increments of 0.1 mJ until no bubble formation is observed. This lower energy level is known as the "treatment energy". Treatment is done in single burst mode placing 50 + 5 contiguous, but not overlapping, 400 um laser spots along 180º. Bubble formation is monitored with each pulse. In cases with significant variation in trabecular pigmentation, the pulse energy is decreased if bubble formation occurred as described above.

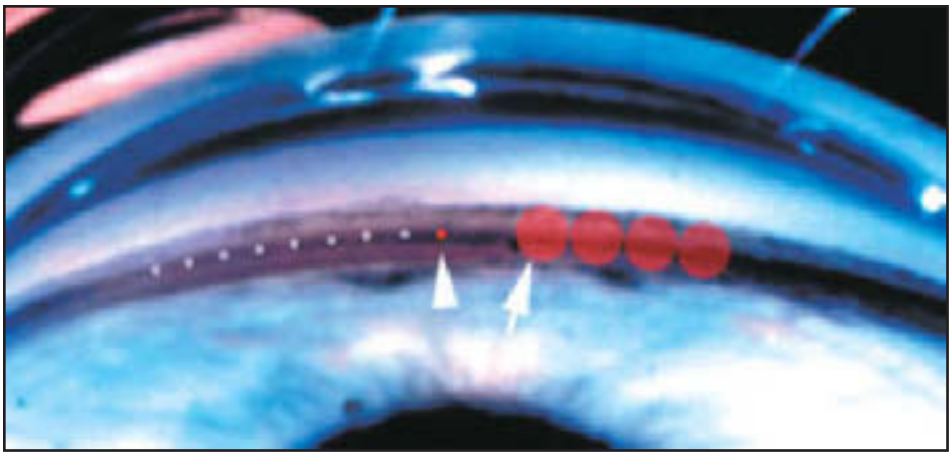


Figure 4. Gonioscopy photograph comparing the spot placements for ALT and SLT. The ALT laser spots (50 um diameter spot size, left arrowhead), are placed in the junction of the anterior one third and posterior two thirds of the TM. On the other hand, the SLT treatment beam (right arrow) measures 400 um and the entire height of the TM can be covered with a single pulse. For both the ALT and the SLT, a total of 50 laser spots are placed to cover approximately 180º of the circumference of the TM (photograph courtesy of Carl Park, MD).

Postoperative Medications

After laser treatment, prednisolone acetate 1% is administered and continued in the treated eye four times daily for 4 days.

Indications

The indications for treatment with Selective Laser Trabeculoplasty (SLT) are similar to the indications for Argon Laser Trabeculoplasty (ALT). Patients with open angle glaucoma who are candidates for conventional ALT can be considered for SLT. In addition, SLT can be a useful treatment alternative in the following subset of patients:

1. Patients who have a history of failed ALT (either 180^{o} or 360^{o}) will respond well with SLT, thus, offering an alternative to patients who would have otherwise undergone incisional surgery.

2. Patients who are poorly compliant or have problems obtaining or intolerant to their glaucoma medications. This treatment option is also reasonable alternative to medications in patients who have a history of poor "follow up" due to personality, economic, or transportation reasons.

3. Because of the non-destructive and potentially repeatable properties of SLT, this treatment modality may be used as a first line treatment for open angle glaucoma. Choosing this treatment option does not affect the success of future surgical procedures. Furthermore, SLT treatment can be repeated a number of times to control the IOP without being concerned about increasing the failure rate of the procedure. This treatment modality has the potential to delay or obviate the need for additional medications and/or incisional surgery in patients with open angle glaucoma

4. SLT has also been shown to work well with patients with pigmentary, pseudoexfoliation, and juvenile open angle glaucomas.

SLT is contraindicated in patients with:

1. Inflammatory/ Uveitic Glaucomas
2. Congenital glaucoma
3. Primary or secondary narrow angle glaucoma
4. Any disease process/ malformation which does not permit the visualization of the trabecular meshwork.

Summary

In summary, Selective Laser Trabeculoplasty is a safe and effective treatment modality for lowering the intraocular pressure in patients with open angle glaucoma. The preservation of the trabecular meshwork architecture and the demonstrated efficacy in lowering the IOP makes the SLT a reasonable and safe alternative to argon laser trabeculoplasty. In addition, SLT is a potentially repeatable procedure because of the lack of coagulation damage to the TM and the demonstrated efficacy in patients with previously failed ALT treatment. Furthermore, SLT can be considered as a primary treatment option in patients who cannot tolerate or are non-compliant with their glaucoma medications, while not interfering with the success of future surgery. Due to its non-destructive properties and low complication rate, Selective Laser Trabeculoplasty has the potential to evolve as an ideal first line treatment in open angle glaucoma.

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Chapter 17
HOLMIUM LASER FILTERING SCLEROSTOMY

Benjamin F. Boyd, M.D., F.A.C.S.
Maurice Luntz, M.D., F.A.C.S.

Dunbar Hoskins, M.D.[1], developed in the early 90's the Holmium laser technique to create a filtering sclerostomy. By this simple procedure it was hoped to bypass the need for a meticulous dissection of conjunctiva. The procedure, therefore, would be especially useful in patients with extensively scarred conjunctiva in whom filtration must be performed in a location like the lower nasal quadrant that is difficult to reach surgically.

Other surgeons have used various forms of laser to create sclerostomies. **Mark Latina, M.D.**, developed an Ab-Interno Laser Sclerostomy. **Latina** used a diode laser with a beam transmitted transcamerally to the chamber angle with the use of a mirrored gonio lens to create a hole in the angle with a resulting filtering bleb without conjunctival dissection. **Wayne March** and **Douglas Gasterland** have used similar procedures.

Hoskins' managed to perform a full thickness laser sclerostomy without much conjunctival dissection by developing a probe that enters a small conjunctival incision 10 or 15 mm from the limbus (Fig. 1). Through this 1mm incision a probe of the Holmium laser, which is a THC:YAG laser, was placed under the conjunctiva and brought up to the limbus (Fig. 1). The helium neon red beam allowed one to see where the laser was aimed. The probe was placed on the limbus and the laser aimed

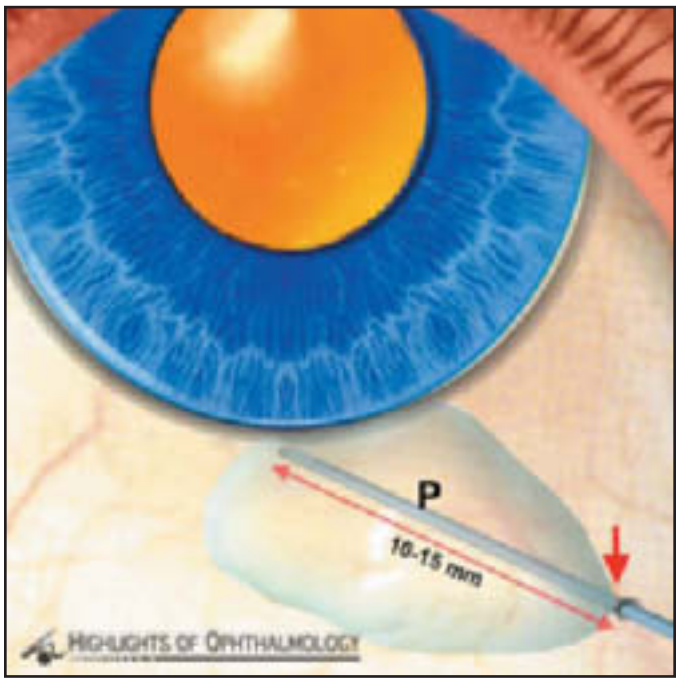


Fig. 1: Full Thickness Filtering Sclerostomy with Holmium Laser - Incision and Positioning of Probe

A one millimeter incision has been made through conjunctiva and Tenon's capsule approximately 10-15 mm from the proposed filtration site (arrow). The conjunctiva is ballooned with saline or viscoelastic creating a tract to the proposed fistula site for insertion of the fiberoptic probe (P). The probe is advanced under conjunctiva until the limbus is reached. The probe's placement should be as anterior as possible without affecting the conjunctiva's insertion. Avoid buttonholing the conjunctiva.

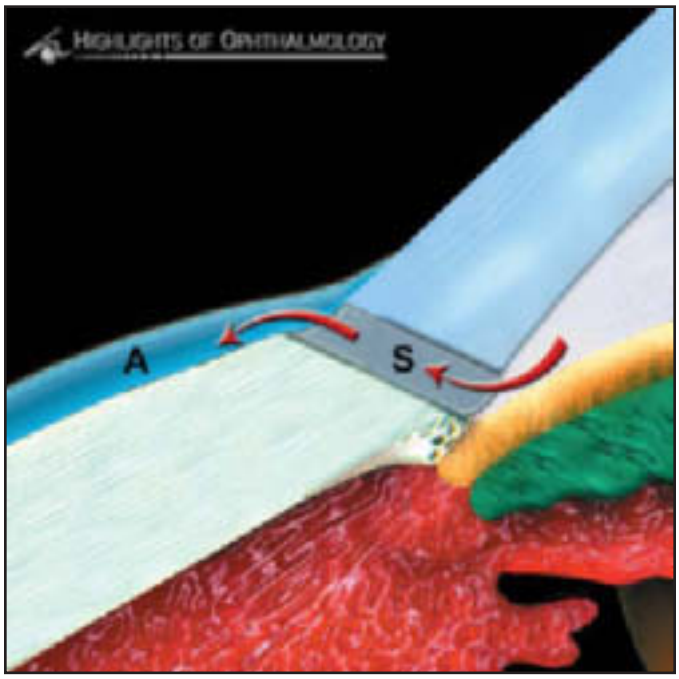


Fig. 2: Full Thickness Sclerostomy with Holmium Laser - Aqueous Moving Through Sclerostomy

As the laser probe is withdrawn aqueous can be seen moving through the sclerostomy (S) to the subconjunctival space (A). There is ballooning of the bleb as the probe is retracted. The conjunctiva is closed with one or two 10-0 nylon sutures. Topical antibiotics and steroids applied.

to direct the beam into the angle of the anterior chamber. The laser was then fired and created an opening into the anterior chamber. On withdrawing the Holmium probe, one usually saw fluid filling the subconjunctival space (Fig. 2). Suturing the small wound completed a rather atraumatic filtration operation. He used antimetabolite (5-FU) injections in combination with the procedure.

Trabeculectomy with Mitomycin C has eclipsed the usefulness of Holmium sclerostomy because it has few postoperative problems and is significantly more successful.

Other Lasers for Glaucoma Filtration

While Holmium laser sclerostomy has fallen into disuse, other lasers for glaucoma filtration surgery have also been explored, particularly the Erbium, Excimer, Nd:YAG and Diode lasers.

The long term results of laser filtering sclerostomy by all these methods have been disappointing and interest in this technique is now almost nonexistent. The excellent results of trabeculectomy with antimetabolites has eclipsed this procedure.

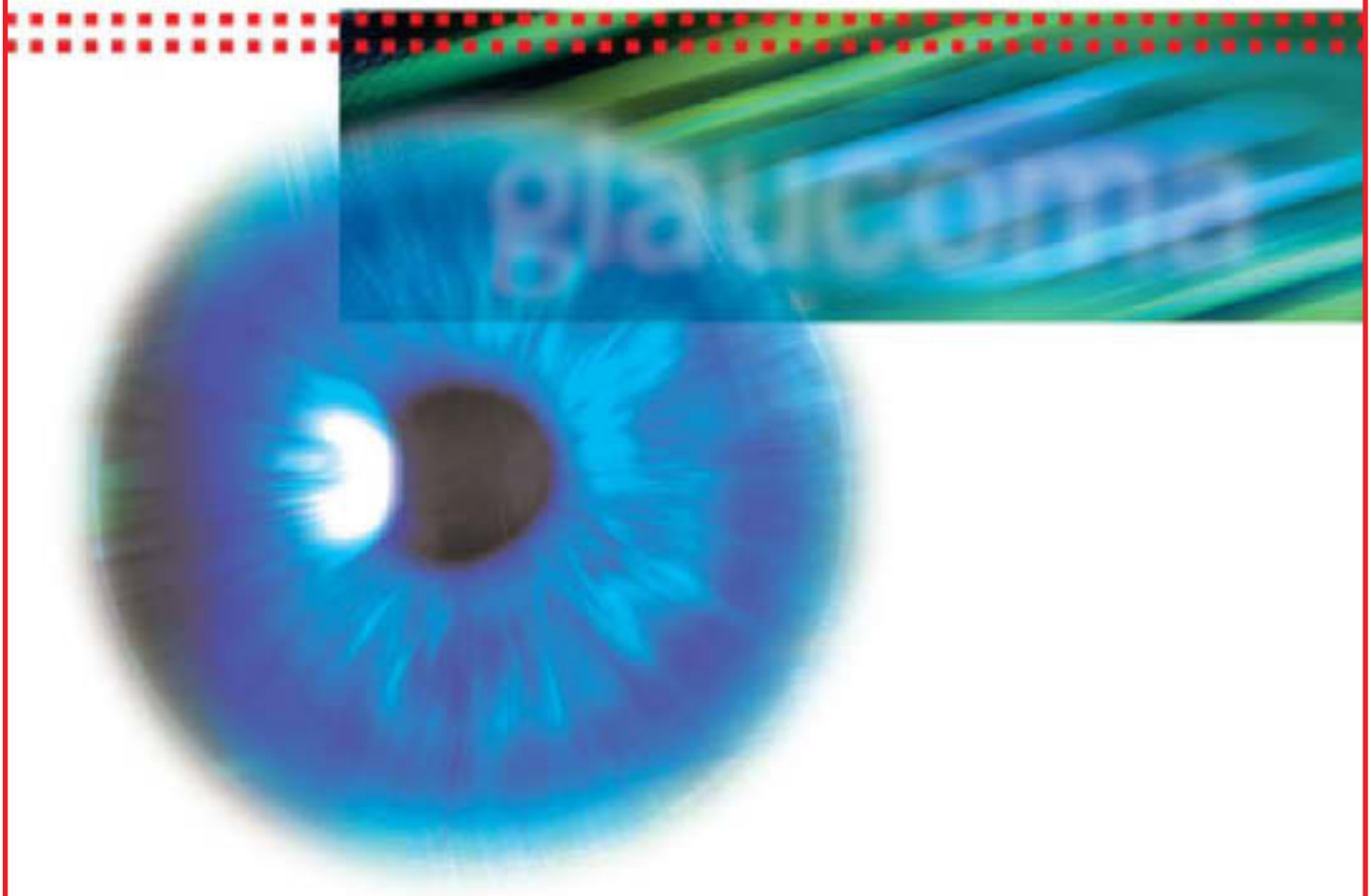
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Incisional Surgical Management

A - Trabeculectomy



Chapter 18
THE CLASSIC TRABECULECTOMY PROCEDURE

Benjamin F. Boyd, M.D., F.A.C.S.
Maurice Luntz, M.D., F.A.C.S.

Indications

Increasing evidence supports the concept that poorly tolerated maximum medical therapy or medical therapy that does not reduce IOP to appropriate levels (target pressure) no longer has a legitimate role in the management of uncomplicated open-angle glaucoma.

There is a fairly strong tendency to consider surgery earlier than we have had in the past. There are several reasons for this:

1) evidence based on the prospective, randomized studies of **Jay**(1) and **Allan** in Glasgow with a mean follow-up of 4.6 years reveals that loss of visual field in patients under medical therapy occur mostly in the first two years after diagnosis while the medical treatment was being modified or until surgery was resorted to in order to aim at achieving the adequate target pressure. (These findings do not reflect negatively on the benefits of medical therapy. The latter have been substantiated through the years. They do reflect negatively on the judgment of many physicians who maintain patients with medical therapy even though the right "target pressure" has not been achieved and hesitate to take the next step, either laser trabeculoplasty or incisional surgery, during long periods in which the patient is maintained at suboptimal pressure levels - **Editor**).

2) Another significant finding in **Jay** and **Allan's** studies is that once there is significant field loss, it becomes more difficult to preserve the remaining fields. When adequate control of intraocular pressure was achieved, however, the reduction in visual fields remained the same in the two groups studied, that is, those treated only with medical therapy vs primary trabeculectomy. However, those with already extensive field loss continued to lose fields slowly despite "normal" intraocular pressures but remained stationary in those with little field loss.

These conclusions reveal the importance of achieving the adequate "target pressure" for each individual patient and not to be misled with a false sense of security, as emphasized by **Al Sommer**(2) and discussed previously. They also explain why we have patients with advanced visual field loss who continue losing fields even though we operate on them successfully.

These findings are reinforced by the studies made at Moorfields in London by **Hitchings** and **Migdal** comparing primary surgery with conventional treatment for primary open angle glaucoma. They have demonstrated **the importance for visual field preservation of reaching a Target Pressure in the mid teens**. These target pressures can be achieved with primary surgery without the use of antifibrotic agents (antimetabolites) and also with medical therapy. The right management of medical treatment

is fundamental for success. Any delay in so doing may increase the risk of visual field loss.

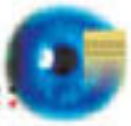
The application of topical medications that contain the preservative benzalkonium chloride may induce chronic episcleral inflammation and perhaps affect surgical results after years of using these medications.

When to Operate

Regarding the fundamental question of how to proceed, and when to perform incisional surgery, **trabeculectomy is not the primary choice on a newly diagnosed case of glaucoma. The initial approach is always to try medical therapy and follow the patient very closely** and over a period of a few months. When we are not satisfied with the level of pressure control and especially when there are changes in the functional status of the eye, then we decide on laser trabeculoplasty or incisional surgery for better control, depending on the disc changes and field loss, and the presence of various risk factors including systemic diseases.

The decision on when to perform a filtering operation also depends somewhat on how close the field loss is to fixation. If there is a threat to central vision we should not wait and must proceed surgically. If the field loss is diffuse and mainly confined to the periphery, well away from fixation, we can wait but observe him/her closely. If the "target pressure" for that patient is not reached and maintained (diurnal pressure checks) with maximum tolerated medication, then ALT is immediately indicated. If this too fails to reach the "target pressure" within a few weeks then a filtering operation is necessary. The danger for the patient is for the ophthalmologist to maintain him/her on a therapy that is not reaching the target pressure for that patient. Indecision or a false sense of security on the part of the physician who maintains the patient on suboptimal levels of intraocular pressure is one of the main factors for continued loss of function. **Hitchings**[3] has emphasized that an eye which deteriorates at a pressure of 18mm Hg is unlikely to slow its rate of decline if treatment only reduces the intraocular pressure to 16mm Hg. The target pressure needs to be lowered if continued field loss occurs. This point is well demonstrated by many studies in the literature -- for example, **Sommer, A.**[4] , in the AJO, 1989, 107: 186-8, concluded that elevated IOP produces optic nerve damage, and that the risk of optic nerve damage increases with increased IOP, even when IOP is under 21mm Hg. There is also the study of Pohjanpelto, P.E., Palva[5] , J., Acta. Ophthal., 1974, 52:194-200, who, in a five-year follow-up of patients, concluded that there was visual field progression over the five-year period in 6% of patients who had a moderately increased IOP, in 28-36% of patients with IOP greater than 30mm Hg, and in 57% of patients with IOP of 40mm Hg or more. Another study to Roth, S.M., Spaeth, G.L., Steinmann, W.C., Poryzees, E.M., Starita, R.J., in Invest. Ophthal. Vis Sci. (Suppl.), 1988, 87:519-25, in an eight-year follow-up of patients, these authors concluded that if IOP averaged 19.3mm Hg 58% of patients showed a progression of visual field loss, and if IOP averaged 14.4mm Hg only 6% showed progression of visual field loss. Hence, the ideal IOP in patients with glaucoma should be 15mm Hg or less.

There is also a tendency for earlier surgical management of glaucoma based on studies that show better stability of IOP control with surgery -- e.g., Odberg, T., in Acta. Ophthal. (Suppl.), 1987, 182:27-29, in a five to 18-year follow-up, concluded that visual fields showed twice the stability in surgically treated eyes compared to medically treated eyes.



Kolker, A.E., in Trans. Am Ophthal. Soc., 1977, 75:539-55, in a four-year follow-up, concluded that visual field loss was progressive in 59% of medically treated patients compared to 23% of surgically treated patients in their study. These studies emphasize that patients with glaucoma and visual field loss should be maintained with IOP in the low teens to put the patient at the lowest possible risk of progressive visual field loss.

Another factor determining a shift to an earlier surgical treatment for glaucoma, or, in some countries, performing surgery as the primary treatment of chronic open-angle glaucoma, is the cost factor. Maintaining patients on long-term medical therapy is expensive and in many poorer countries not feasible.

FILTERING OPERATIONS

THE CLASSIC TRABECULECTOMY PROCEDURE

Trabeculectomy With Fornix Based Flap

The most frequently performed operation for open angle glaucoma is trabeculectomy[1] . **Maurice Luntz, M.D.**, popularized the trabeculectomy with fornix based conjunctival flap and tightly sutured scleral flap[2] years ago by demonstrating its advantages and effectiveness in white as well as South African blacks (Fig. 1)[3] . This procedure is a keratectomy and trabeculectomy extending to the scleral spur and covered by a half-thickness scleral flap (Fig. 6) which is tightly sutured back into place and can be used in standard open angle glaucoma cases as well as in eyes with glaucoma and cataract. Presently, the use of releasable sutures for the scleral flap is preferred.

Advantages of Fornix-Based Flap Trabeculectomy

The advantages of this technique over the limbus based flap trabeculectomy are as follows:

1) There is better exposure and visualization of the operating field. Dissection of the scleral flap well into the cornea is facilitated (Figs. 6, 10,11). This insures a trabeculectomy well in front of the root of the iris and ciliary body and reduces the possibility of hypertrophic ciliary body pigment or iris adhesions obstructing the trabeculectomy opening.

2) The procedure is technically easier than dissecting a limbus based flap, especially when operating in an area of scarred conjunctiva, from either previous trauma or surgery.

3) The possibility of damaging the conjunctival flap during dissection, especially button-holing the flap, is eliminated.

4) The conjunctival flap adheres to and scars at the limbus. The subconjunctival bleb that results is pushed posteriorly producing a diffuse, well vascularized thicker-walled bleb in the upper half of the conjunctiva. There is little possibility of developing a thin, avascular bleb anteriorly placed and overhanging the cornea.

5) The scleral flap is sutured back into place. The flap prevents excessive aqueous humor filtration and maintains the anterior chamber postoperatively.

6) The same technique can be effectively used for combined cataract surgery and trabeculectomy with all its advantages. The risk of shallow or absent anterior chamber postoperatively is considerably less with this method.



Fig. 1: Trabeculectomy with Fornix Based Flap:

A fornix based flap (X) is dissected at the limbus (L) for a length of 7 mm. The conjunctiva is dissected back in a plane between the conjunctiva, episclera and sclera up to the initial fornix based incision (X), 4 mm behind the limbus.

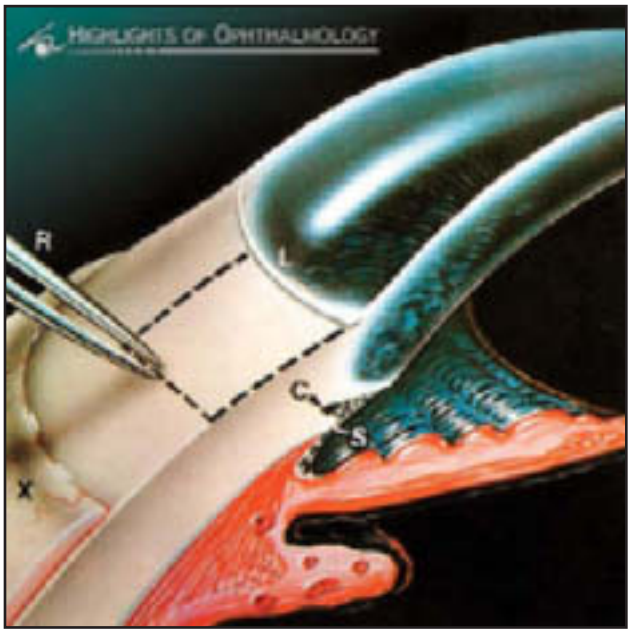


Fig. 2: Trabeculectomy with Fornix Based Flap - Outlining the Scleral Flap - Anatomical Relations with Angle Structures

The scleral surface is cleaned and a 3 mm x 3 mm scleral flap hinged at the limbus (L) is outlined with cautery (R), (dotted line). Fornix based conjunctival flap (X). The Canal of Schlemm (C) is shown lying over the trabeculum and scleral spur, (S).

Surgical Technique 1

Conjunctival Flap (suggest 5x magnification)

A fornix based conjunctival flap 7 mm long is fashioned at the limbus (Fig.1). The conjunctiva is dissected back in a natural surgical plane between the conjunctiva, episclera and sclera. Any bleeding points on the conjunctiva or sclera are dealt with at this stage.

Dissection Scleral Flap (suggest 10x magnification)

The scleral surface is cleaned and a 3 mm x 3 mm scleral flap is outlined with cautery in the bare area of the sclera (Fig. 2). This flap is hinged at the limbus which insures that the conjunctival and

scleral suture lines are separated. The anatomical relationships of the scleral flap are shown in Fig. 3 (A-B).

The scleral flap is incised with two half-thickness scleral incisions 3 mm apart extending back 3 mm from the limbus (Fig. 4). These are joined

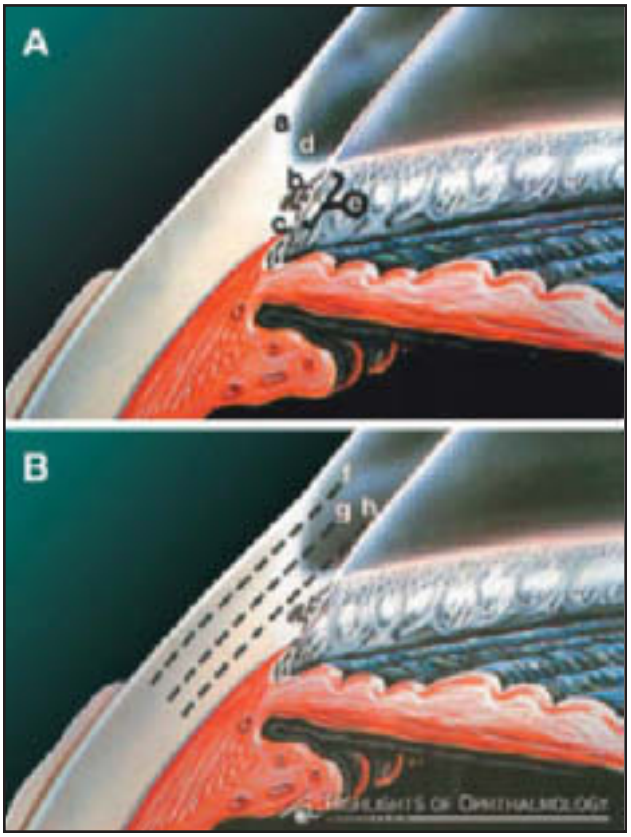


Fig. 3: Anatomical Relationships for the Scleral Flap in Trabeculectomy

These anatomical relationships are of great value as a guide to localize the trabeculectomy opening in the right place and in performing the desired-thickness scleral flap. **Fig. (A)** Near the corneo-scleral junction, the three finger-like anterior digitations of the sclera are noted (a), (b) and (c). (c) is the scleral spur. The corneal border in the form of a wedge is indicated at (d). The Canal of Schlemm and trabeculum are shown at (e). **Fig. (B)** The scleral flap for trabeculectomy can vary in thickness, as follows, in relation to the anatomical structures shown in Fig. (A); (f) Very thin scleral flap entering the cornea above and anterior to the blunt tip of the corneal wedge. This type of flap is undesirable. (g) Half thickness scleral flap penetrating corneal tissue approximately at the vertex of the corneal wedge. This is the most desirable flap. (h) Extremely thick scleral flap penetrating the cornea below and a little advanced to the vertex of the corneal wedge. This flap is also undesirable.

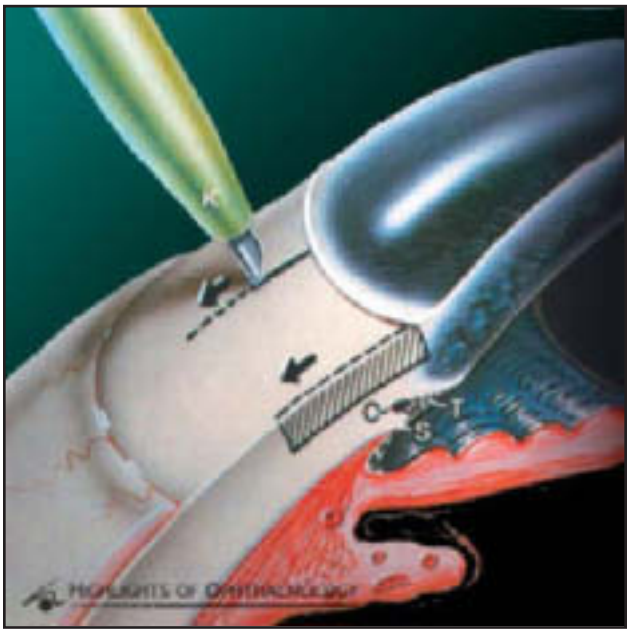


Fig. 4: Trabeculectomy with Fornix Based Flap - Incising the Scleral Flap

The scleral flap is incised with two half-thickness incisions radially. Scleral knife (K). The depth of these incisions is denoted by the cross-hatched area on the scleral cross section. The Canal of Schlemm (C) is indicated lying over the trabeculum (T) and scleral spur, (S).

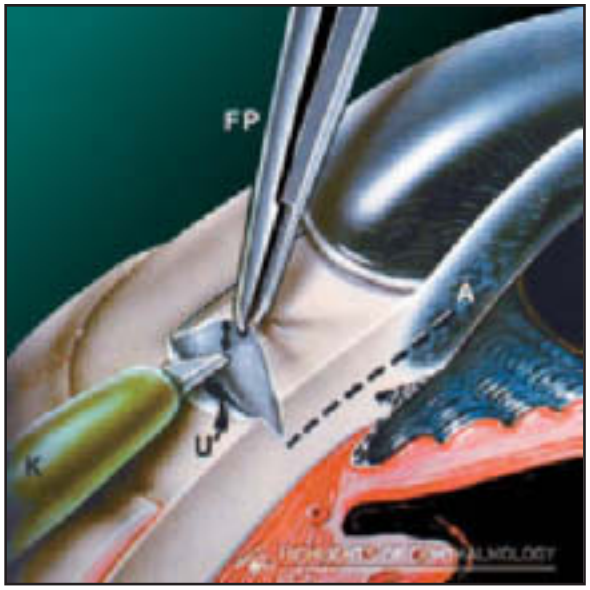


Fig. 5: Trabeculectomy with Fornix Flap-Beginning the Scleral Flap Dissection

The two radial incisions are joined posteriorly with a scleral incision extending down to the level of the choroid at one spot, (U). With the full thickness of the sclera observable by lifting this posterior incision with forceps (FP), the desired thickness for the scleral flap is determined. This is predetermined by performing a half-thickness (small double arrows) scleral flap. With the knife (K), dissection of the scleral flap is commenced. Staying in the same surgical plane, the dissection is carried forward (along the dotted line) into the cornea at point (A).

by a 3 mm long incision posteriorly which is dissected down to the level of the choroid (Fig. 5). The thickness of the sclera can be estimated from the posterior incision, allowing accurate dissection of scleral flaps of varying thickness. The thickness chosen for the scleral flap depends on the pathology and the prognosis for surgery. Ideally, the flap should be half the scleral thickness which permits adequate aqueous filtration but avoids the possibility of an excessively thin scleral flap becoming staphylomatous. The dissection of the scleral flap is commenced from the posterior incision at the desired thickness and, staying in the same surgical plane, it is carried forward into the cornea to just within the surgical limbus (Figs. 5 and 6).

Under the scleral flap, the salient external landmarks are easily recognized in the undissected scleral portion (Fig. 6) anteriorly, transparent, deep

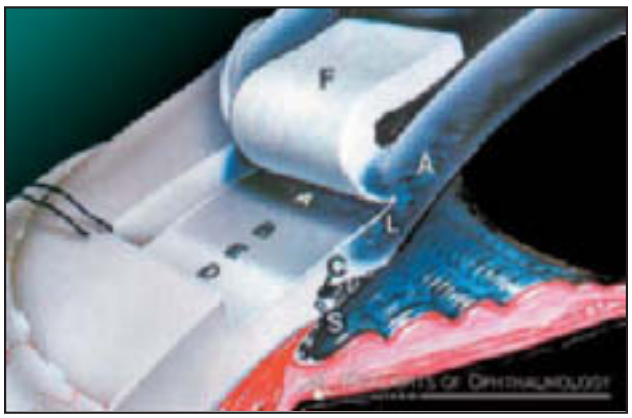


Fig. 6: Trabeculectomy Gonioscopic View - Relationships of Internal Structures to External Landmarks.

Relationships to external landmarks seen in Fig. 7 include (A) - transparent cornea; (B) - trabeculum (gray band); (D) - white opaque sclera. The junction of the trabeculum gray band (B) with the white opaque sclera (D) denotes the deeper scleral spur (S) which is seen as (E) externally. Scleral flap (F), Canal of Schlemm (C). The external limbus is denoted as a dotted line (L) in clear cornea, (A).

corneal tissue; behind this, a gray band of parallel-layered tissue which overlies the trabecular meshwork and merges into white, opaque sclera with crisscrossing fibers. At the junction of the gray trabecular band and the sclera is the scleral spur and Schlemm canal. This external landmark for the scleral spur (the junction of the posterior border of the trabeculum band and the sclera) is by far the most important surgical landmark. It indicates the site of the scleral spur and thus the posterior limit of the corneo-trabecular tissue removed in a trabeculectomy and it also indicates the approximate location of the Canal of Schlemm.

The relationship of the internal structures to the external landmarks involved in a trabeculectomy operation are shown in a gonioscopic view in Fig.7.

Schlemm's canal is anatomically related to the scleral spur. In some eyes, it is situated just anterior to the scleral spur and is then found histologically in the trabeculectomy specimen. In others, it lies at or behind the scleral spur. In the former case, it is difficult to identify histologically in the trabeculectomy specimen; in the latter case, it is not in the trabeculectomy specimen. In Fig. 7. Schlemm's canal is indicated lying in front of the scleral spur.

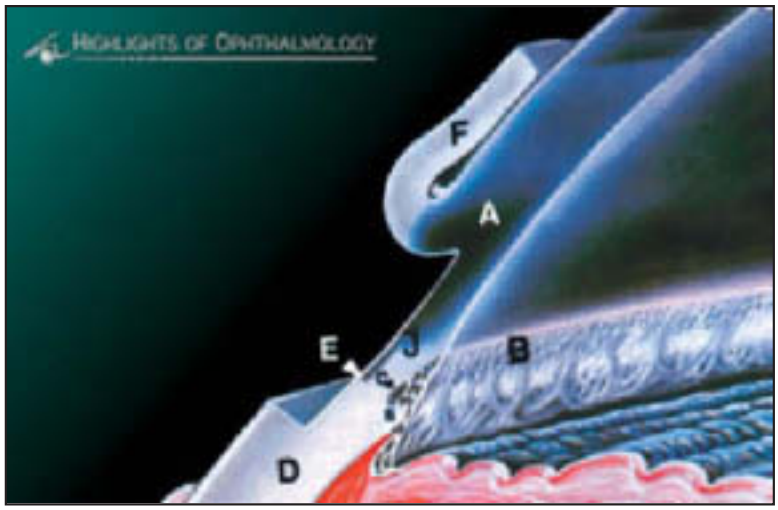


Fig. 7: Trabeculectomy Surgical and Anatomical Landmarks

The half-thickness scleral flap (F) is reflected. (A) - transparent cornea; (B) - gray band (trabeculum); (D) - white opaque sclera. The junction of the gray band (B) and the sclera (D) denotes the external location (E) of the deeper scleral spur (S). Schlemm's Canal (C) is anatomically related to the scleral spur (S). Corneo-scleral junction (J).

Trabeculectomy Opening (suggest 10x magnification)

The next step is to outline a 2 mm x 2 mm square of cornea and trabeculum in the undissected cornea and sclera deep to the scleral flap extending anteriorly from the limbus back to the scleral spur and hinged at the scleral spur, incising to 1/2 the depth of this tissue (Fig. 8). The anterior incision is made at the surgical limbus which is well into the deeper layers of the cornea (Fig. 8). On postoperative gonioscopy, the trabeculectomy opening can be seen to extend well into the posterior corneal surface and well clear of the iris (Fig.13). The side incisions extend back to the scleral spur. No posterior incision is made at this time. With the internal flap outlined, the anterior incision is dissected through Descemet's membrane into the anterior chamber which is not lost at this stage as iris will plug the incision. A Vannas scissors is carefully introduced and the anterior incision completed still without losing the anterior chamber. This is extended along the sides, cutting back to the external landmark for the scleral spur (Fig. 9).

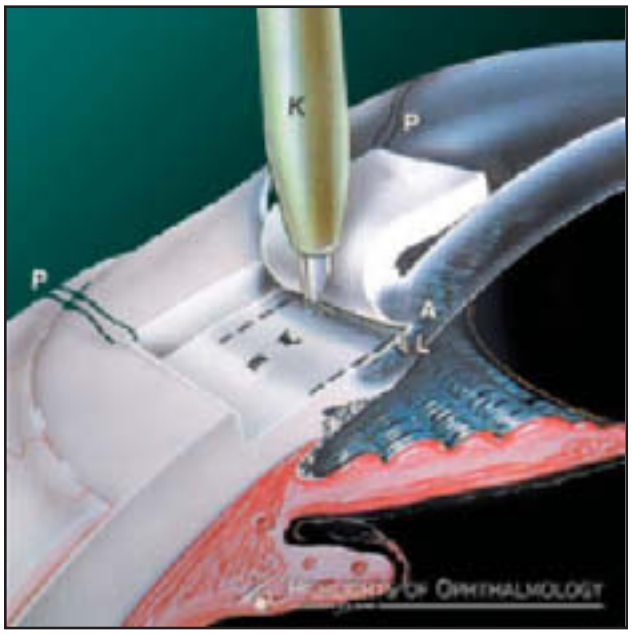


Fig. 8: Trabeculectomy with Fornix Based Flap - Outlining the Tissue Window to be Removed

A 2 mm x 2 mm square cornea and trabeculum is outlined with a sharp knife (K). This tissue to be removed (W) extends anteriorly from the surgical limbus (L), which is well into the deep layers of the cornea (A), posteriorly to the scleral spur (S), indicated by the posterior border of the gray band (E). This window is incised one half the depth of this tissue, making an anterior cut along the limbus and two side cuts each extending posteriorly to the external landmark for the scleral spur, (E). No posterior incision is made at this stage. 10-0 nylon sutures (P) should be pre-placed at the posterior corners of the scleral flap and the scleral bed and moved out of the way.

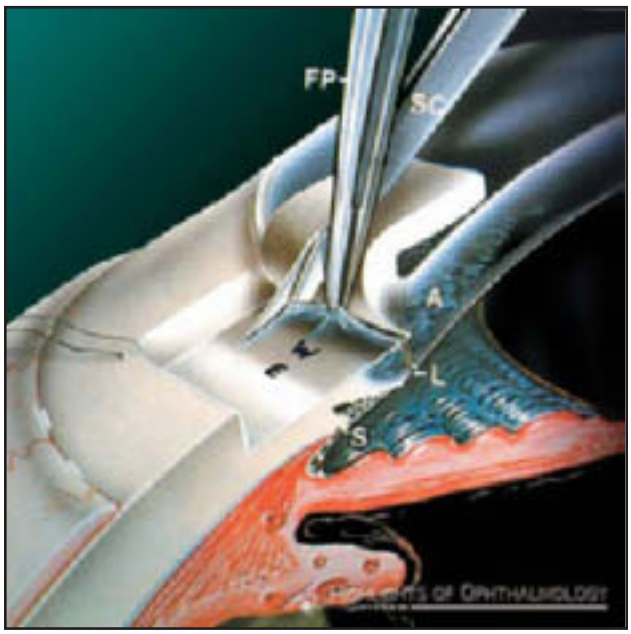


Fig. 9: Trabeculectomy with Fornix Based Flap - Extending the Window Along the Sides

With the knife, the anterior incision at the limbus (L) which is in clear cornea (A), has been dissected through Descemet's membrane into the anterior chamber. Using Vannas scissors (SC) the anterior incision is completed. The radial incisions (shown here) are made through the trabeculum (W) to the external landmark (E) representing the scleral spur (S). Forceps, (FP).

The flap is removed by a posterior incision just in front of the scleral spur, visualizing the scleral spur by rotating the flap posteriorly (Figs. 10, 11, 12).

An iridectomy is now made. It is imperative that the iridectomy be wider than the trabeculectomy opening so that iris pillars are not pushed into this

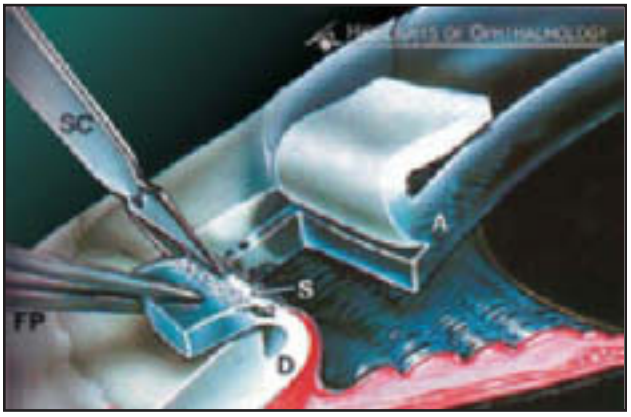


Fig. 10: Completing the Trabeculectomy Opening

A posterior incision of the trabeculectomy flap is made just in front of the scleral spur (S) using Vannas scissors, (SC). This completes the excision of the flap of Trabeculum and cornea. The scleral spur, (S), is visualized by rotating the Trabeculectomy flap posteriorly with forceps (FP) so that one is looking directly at the scleral spur (S). Junction of gray band (B) and white opaque sclera (D) is noted at (E), which is the external landmark for the scleral spur. Clear cornea (A). Externally, the gray band (B) reveals the location of the deeper trabeculum.

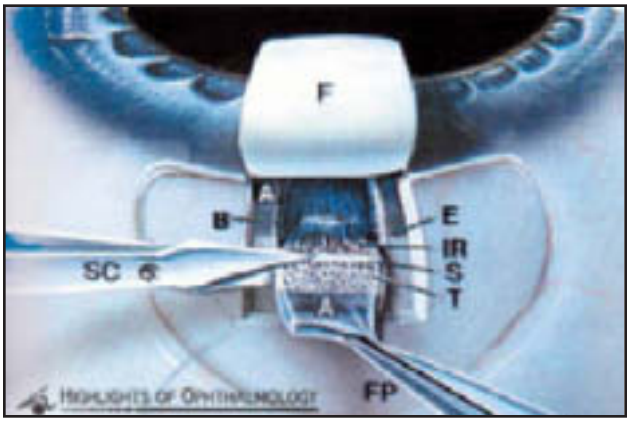


Fig. 11: Trabeculectomy with Fornix Based Flap - Removing the Trabecular Window - Surgeon's View

This is a surgeon's view of the final incision to remove the trabecular window, as seen in Fig. 10. It also reveals the surgeon's view of the structures most important to proper trabeculectomy. The Trabeculectomy flap which is being excised has been hinged backwards exposing its deep surface to the surgeon's view. The Vannas scissors (SC), make the final cut just in front of the scleral spur (S), on the trabecular tissue which is here being reflected back with forceps (FP). The scleral spur is localized externally (E) by the junction of white sclera and gray band (B). Scleral flap (F). Clear cornea (A). Iris (I). Iris root (IR). Trabeculum (T).



Fig. 12: Exposure of Vital Structures Through Trabeculectomy

Final location of the "window" in relation to the trabecular structures. Insertion of ciliary muscle (M) remains intact at the scleral spur (S). Canal of Schlemm not visible in this view. It is placed just anterior to the scleral spur and has been partially removed with the excised cornea and trabeculum. Trabeculum (T) along the radial wall of the "window". Junction of sclera and cornea, (J). Clear cornea (A).

Adjacent to the radial wall of the excised "window" is an unexcised portion of the bed of the lamellar scleral flap which demonstrates the external landmarks for these internal structures. Clear cornea (A), gray band which is the external landmark for the trabeculum (B). External landmark for scleral spur (E). The scleral spur (S) lies in relationship to "E".

On the opposite side of the "window", the radial wall has been removed. Anterior incision lies in clear cornea. Posterior incision lies immediately in front of scleral spur. A portion of the posterior trabeculum in the sclera just behind this posterior incision of the "window". This good exposure is made possible with a fornix based conjunctival flap.

opening postoperatively (Fig. 13). This is achieved by grasping the iris with forceps, moving it to the left and commencing an iridectomy incision with scissors from the right side (Fig. 13). As this incision approaches the midway point of the iris, the iris is moved across to the right and put on stretch and the incision is completed toward the left side.

As the iridectomy is completed, the anterior chamber may be lost and can be maintained with air or Healon.

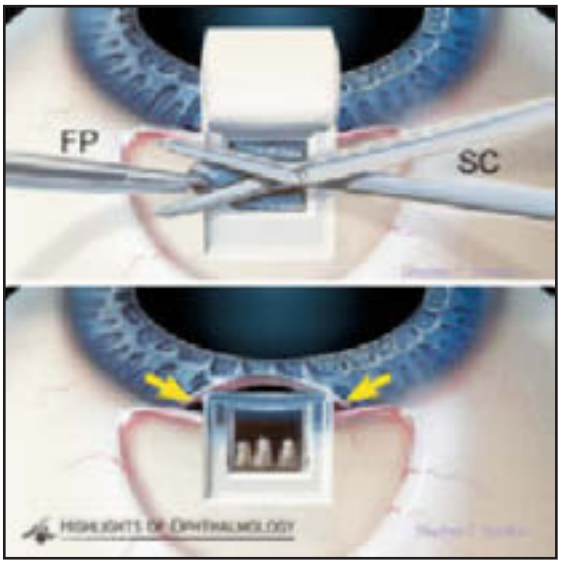


Fig. 13: Trabeculectomy with Fornix Based Flap - Performing the Iridectomy

An iridectomy is performed through the excised "window" of cornea and trabeculum. The iridectomy must be wider than the trabeculectomy opening so that iris pillars are not pushed into this opening postoperatively. (Above): the iris is first grasped with a forceps (FP) and pulled to the left while cutting with a scissors from the right side (SC). (Below): the iridectomy boundaries, indicated at the arrows, go beyond the edges of the trabeculectomy opening.



Fig. 14: Trabeculectomy with Fornix Based Flap - Final Configuration - Inner View

This internal cross-section view reveals the final configuration once the external partial-thickness scleral flap (F) is repositioned into its scleral bed and the 10-0 nylon sutures (P) at the posterior corners of the flap are tied. Iridectomy is at (I). Trabeculectomy window is at (W). The Canal of Schlemm (C) is indicated lying anterior to the scleral spur (S) and has, therefore, been included in the corneo-trabeculectomy excision.



Fig. 15: Trabeculectomy - Final Configuration - Surgeon's View

The scleral flap is sutured with six 10-0 nylon sutures (see also Fig.16). These sutures may be removed later with the argon laser applied through the conjunctiva if increased flow of aqueous is desired (Laser Suture Lysis). In (B) is shown the recommended 1/2 thickness of the scleral flap. In (A) is shown a thinner flap which is not recommended.

Suturing Lamellar Scleral Flap (suggest 5x magnification)

Follow the same technique as in Surgical Technique Trabeculectomy 3. The use of releasable sutures is the preferred suturing technique.

The conjunctiva is rotated anteriorly to the limbus and sutured with two 10-0 nylon sutures placed through the conjunctiva and sclera at each end of the conjunctival flap, pulling the conjunctival edge taut along the limbus (Fig. 16).

Balanced salt solution is injected under the conjunctival flap to lift it from the sclera. The patient leaves the operating table with an intact anterior chamber and a bleb at the site of the trabeculectomy. If the surgeon decides to use Viscoelastics in the anterior chamber during the procedure, it should be removed at the end of the operation to avoid elevation of the intraocular pressure postoperatively. (See "Use of Viscoelastics with Trabeculectomy" in this same Section).

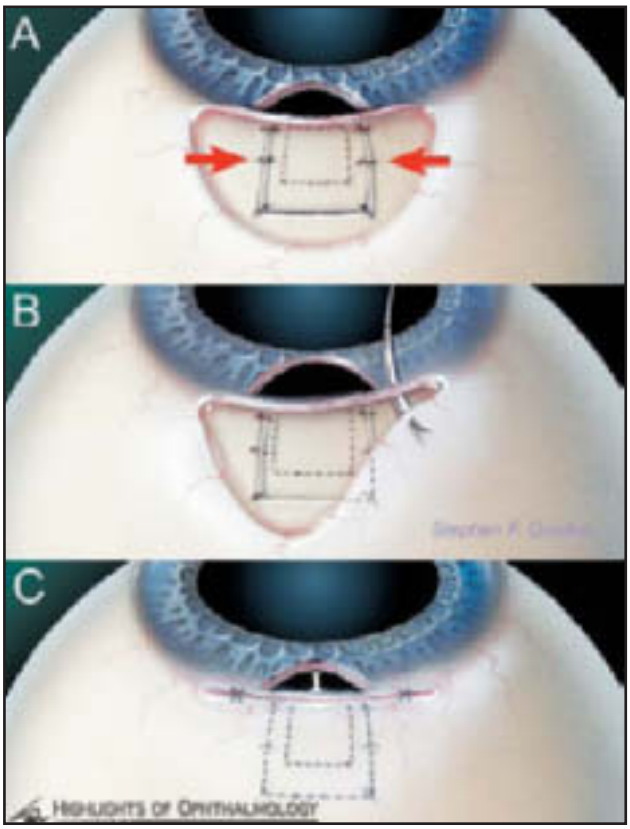


Fig. 16: Trabeculectomy with Fornix Based Flap - Conjunctival Closure

These series of steps demonstrate the technique of conjunctival closure. (A) Additional 10-0 nylon sutures have been added to the now closed partial-thickness scleral flap, one pair (arrows) midway between the anterior and posterior ends of the radial flap incisions. Another pair of sutures have been added near the limbus. The 2 x 2 mm trabeculectomy "window" is shown as a dotted line, located deep to the external scleral flap. (B) The conjunctiva is rotated anteriorly to the limbus and sutured with two 10-0 nylon sutures, placed at each end of the conjunctival flap as shown and anchored in superficial lamellae of sclera. (C) The final configuration demonstrates the conjunctival flap sutured to the sclera. Iridectomy located at (I).

Trabeculectomy with Limbus Based Flap

Surgical Technique 2

The technique for this commonly performed procedure is shown in Figs. 17, 18, 19, 20, 21. This method has the slight disadvantage of being technically somewhat more difficult than when dissecting a fornix based flap, especially when operating in an area of scarred conjunctiva. There is also the possibility of button-holing the flap.

The actual trabeculectomy, cutting out about a one by two millimeter flap of the trabecular meshwork, may be done with a sharp blade, as shown previously for the fornix based conjunctival flap technique, (Figs.1 through 16) or with a trephine, as shown here in Figs. 18 through 21. The trabeculectomy block should be removed anterior to the scleral spur. By leaving the scleral spur undisturbed, there is far less bleeding and you avoid a cyclodialysis effect that cuts down filtration through the cleft in the early postoperative period.

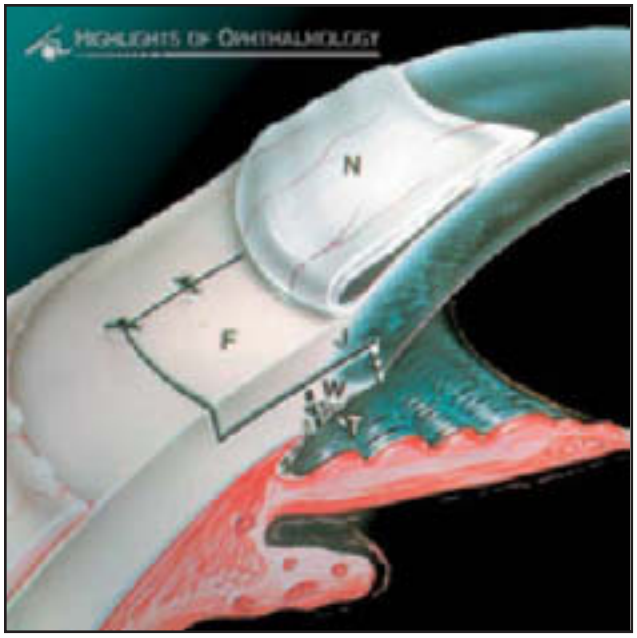


Fig. 17: Trabeculectomy With a Limbus Based Flap - Anatomical Relationships

The trabeculectomy "window" (W) is shown here in place but this is the block of tissue actually removed. A half thickness scleral flap (F) has been sutured back into place. A limbus based conjunctival flap has been used (N). The Canal of Schlemm has a variable relationship to the scleral spur; it may lie anterior to the spur, at the spur or behind the spur or overlap the spur. Thus the Trabeculectomy "window" may or may not include the Canal of Schlemm depending on the situation of the Canal. In this illustration, the Canal of Schlemm lies behind the scleral spur (S) and trabeculum (T). The corneal-scleral junction is seen in (J).

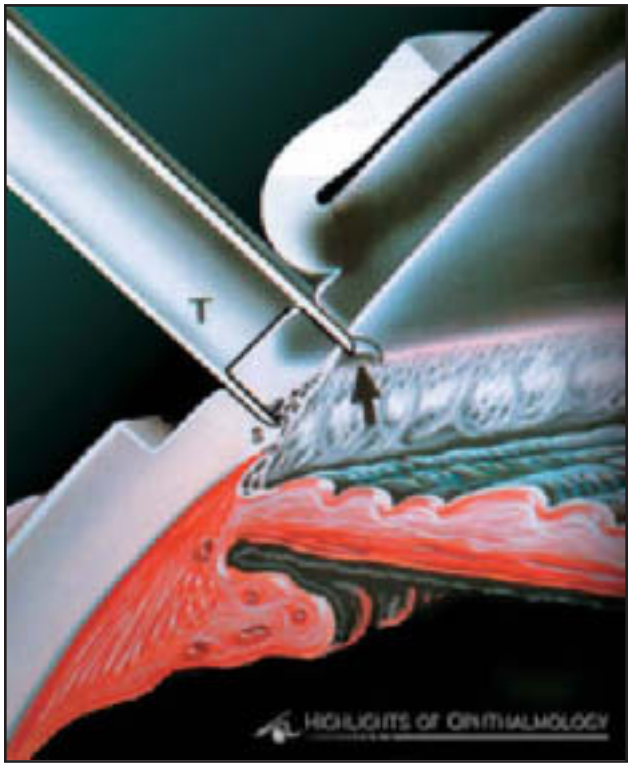


Fig. 18: Trabeculectomy With a Limbus Based Flap Performed With Trephine

When using a trephine to perform a trabeculectomy, it is advised to perforate the anterior chamber along the corneal side first rather than 360º all at once. Here the trephine (T) is titled forward. The trephine is seen penetrating (arrow) the anterior chamber along the corneal side first. As soon as aqueous oozes out, the trephine is withdrawn and the operculum is completed with a sharp razor. This is done to carefully inspect, under high magnification, proper localization of the operculum with reference to the scleral spur (S), so as not to excise the spur.

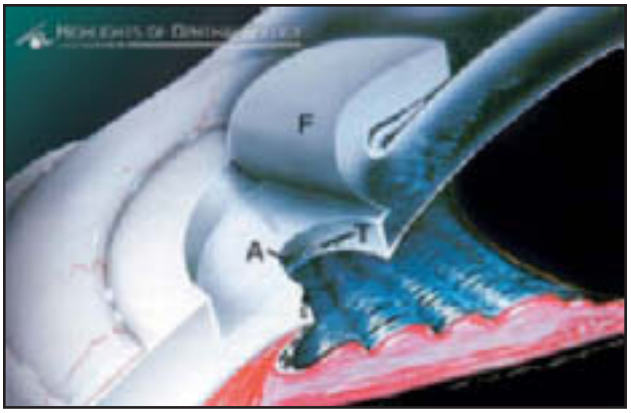


Fig. 19: Trabeculectomy With Limbus Based Flap - External Cross Section View – Anatomical Relationships

The trabeculectomy performed with the trephine is complete as seen from the external perspective. The trephined operculum has incorporated a portion of the Canal of Schlemm (A) and the subjacent trabeculum (T). Corneo-scleral lamella (F). The scleral spur (S) lies intact at the posterior edge of the operculum.



Fig. 20: Trabeculectomy With Limbus Based Flap. Gonioscopic Cross Section View

The final removed operculum is shown in relation to the angle structures visible in a gonioscopic view. The partially excised Canal of Schlemm (A) is visible. The area of removed trabeculum is also visible. Intact scleral spur (S).

Use of Viscoelastics in Trabeculectomy

Viscoelastics may be injected in the anterior chamber during trabeculectomy to significantly decrease the complication rate. Some surgeons use viscoelastics during glaucoma surgery not only in the anterior chamber but also under the conjunctival flap with the intent to increase the rate of successful post-operative diffuse filtration blebs.

Richard Wilson, organized and directed a case control study containing 119 consecutive cases using viscoelastics and the previous 122 consecutive cases without viscoelastics. The operation performed was a standard limbus-based trabeculectomy. The object of the study was to determine if the use of viscoelastics would be helpful in improving the long-term success rate of trabeculectomy and in decreasing the complication rate, and whether the substance would have any objectionable side-effects.

Dr. Wilson[8] found that, not only at six months but also at an average of fourteen months, there was no appreciable difference between the two groups with respect to intraocular pressure, the number and strength of medications necessary to control the pressure postoperatively, or the small change in vision after surgery. There were, however, **significant beneficial effects from viscoelatics in lowering the complication rate**.

If there is bleeding at the time of excision of the scleral block or iridectomy, then a viscoelastic should be injected immediately. This pushes blood from the anterior chamber out the cleft, raises the intraocular pressure and usually stops the bleeding. The use of viscoelastics does not improve the results of intraocular pressure control nor the percentage of diffuse filtering blebs obtained.

THE TUNNEL SCLERAL INCISION TRABECULECTOMY

Surgical Technique 3

The Tunnel Scleral Incision Trabeculectomy is Dr. Luntz' preferred technique. All three techniques have essentially the same results when properly done. Which one to perform depends on the individual surgeon's particular inclination.

Maurice Luntz, M.D., F.A.C.S - Director of the Glaucoma Service at Manhattan Eye, Ear & Throat Hospital in New York, and **Abraham Schlossman, M.D.**, attending Manhattan Eye, Ear and Throat Hospital, have developed a modified trabeculectomy using a "tunnel" scleral incision based on the type of incision utilized in cataract surgery with phacoemulsification.(6) This tunnel scleral incision trabeculectomy has excellent result, at least comparable to those obtained using the standard trabeculectomy technique originally described by Cairns(7) but, in addition, has one advantage: it considerably simplifies the dissection of the lamellar scleral flap with extremely smooth surfaces. This tunnel incision which is preferred to the standard incision is the same incision made for phacoemulsification cataract extraction, so that any surgeon using this latter technique is familiar with it.

Dissection of the sclera with the crescent knife to make a tunnel is an easier method of dissecting a lamellar scleral flap (which is completed by two radial incisions with Vannas scissors) than the standard method which requires knife dissection of the scleral flap starting 2.5 mm behind the limbus and dissecting to the limbus. The tunnel incision is completed by entering the anterior chamber with a 3.2 mm keratome, an easier technique than dissecting through the deep scleral base into the AC as is done in the standard technique.

The inner surface of the lamellar scleral flap and the surface of the deep scleral base are much smoother with the tunnel incision than can be achieved by dissecting in accordance with the standard method.

SURGICAL TECHNIQUE

Conjunctival Flap (suggested magnification 5x)

A 5 mm wide, fornix-based conjunctival flap is raised at the limbus in the superonasal quadrant. The advantages of a fornix-based conjunctival flap are: 1) the Tenon's fascia is minimally traumatized; 2) there is better exposure of the limbal area; and 3) thinning of the limbal conjunctiva and overhang of the cornea are avoided. With the conjunctival flap pushed posteriorly, hemostasis of exposed sclera is obtained.

Tunnel Incision (suggested magnification 10x)

Using a crescent knife (Alcon), an incision is made parallel and 2 mm posterior to the limbus, extending 3 mm in width (Fig. 21). The incision is carried down to about one-third of the scleral thickness (Fig. 22). The same knife is introduced at the base of this incision and dissects anteriorly toward the limbus (Fig.22), extending into the cornea just anterior to the vascular arcade, forming an intracorneal pocket at about one-third scleral depth with a width of 3 mm. A 3.2 mm keratome is introduced into the scleral pocket and advanced to its anterior edge immediately anterior to the limbal-corneal vessels. The point of the keratome is then depressed and the keratome advanced into the anterior chamber for its full length, directed parallel to the plane of the iris, producing a 3.2 mm wide incision (Fig. 22). This maneuver completes a tunnel incision into the anterior chamber.

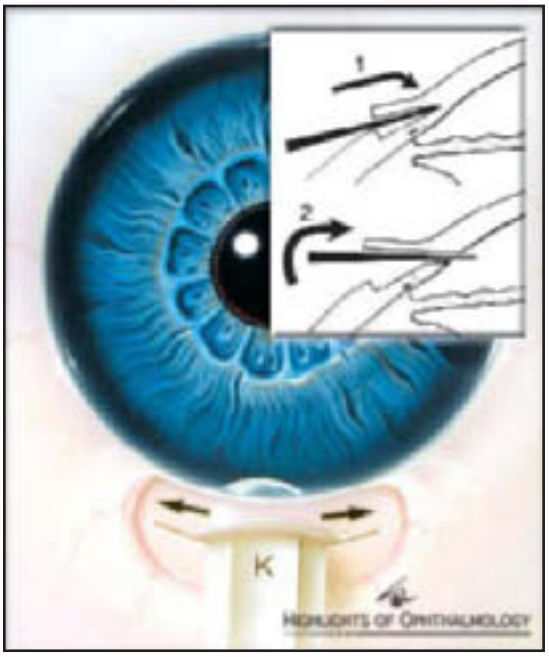


Figure 22: Modified "Tunnel" Trabeculectomy Technique - Step 2 - Tunnel Incision

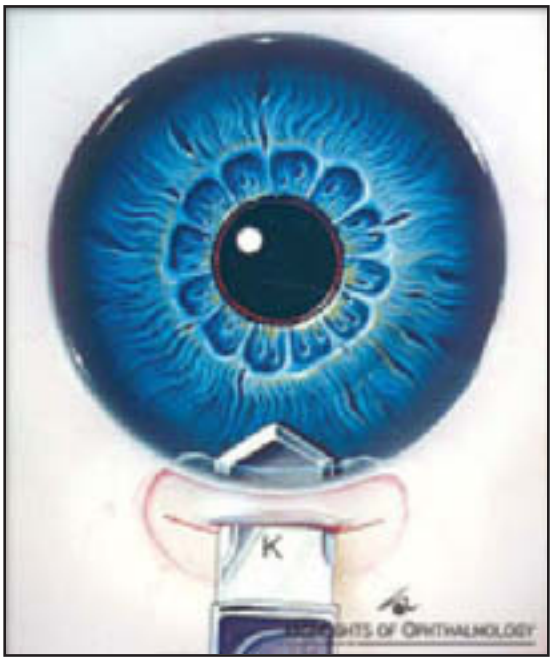
A 3.2 mm keratome (K), is introduced into the scleral pocket and advanced into the anterior chamber, directed parallel (arrow) to the plane of the iris. This will produce a 3.2 mm wide incision, completing the tunnel incision into the anterior chamber.

Figure 21: Modified "Tunnel" Trabeculectomy Technique - Step 1 - Conjunctival and Initial Incision

A 5 mm wide, fornix-base conjunctival flap is raised at the limbus in the superonasal quadrant. A Crescent knife (K) then makes an incision 2 mm posterior to and parallel to the limbus extending 3 mm in width. The incision is perpendicular to the sclera and carried down to about 1/3 of the scleral thickness.

This cross section view shows the fornix-based conjunctival flap and the initial incision made with the Crescent knife (K). Notice that this incision is 2mm posterior to the limbus and extends to a depth of 1/3 the thickness of the sclera (arrows - inset).

The Crescent knife (K) is then introduced at the base of the initial incision and dissects anteriorly toward the limbus (arrows), extending into the cornea just anterior to the vascular arcade. This will form an intracorneal pocket at about 1/3 scleral depth and with a width of 3mm.



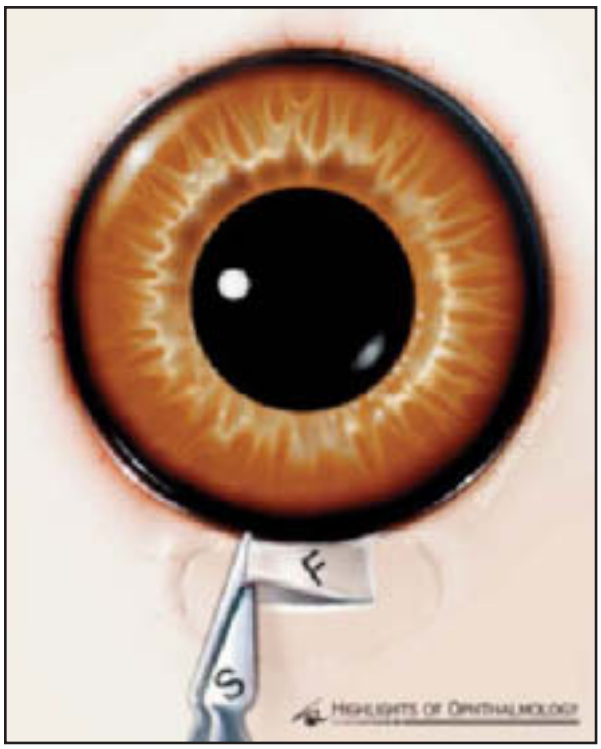


Figure 23: Modified "Tunnel" Trabeculectomy Technique - Step 3 - Lamellar Scleral Flap

A Vannas scissors (S) is used to fashion a radial incision at each side of the tunnel, to form the lamellar scleral flap. The resulting flap (F) is 3.2 mm wide by 2mm antero-posterior.

Forming the Lamellar Scleral Flap (suggested magnification 5x)

A Vannas scissors is used to fashion a radial incision at each side of the tunnel (Fig. 23), producing a 3.2 x 2 mm lamellar scleral flap.

Trabeculectomy (suggested magnification10x)

The lamellar scleral flap is raised, exposing the underlying sclerocorneal bed. A Luntz-Dodick punch is advanced to the anterior edge of the sclerocorneal bed (Fig. 24), and corneoscleral tissue is

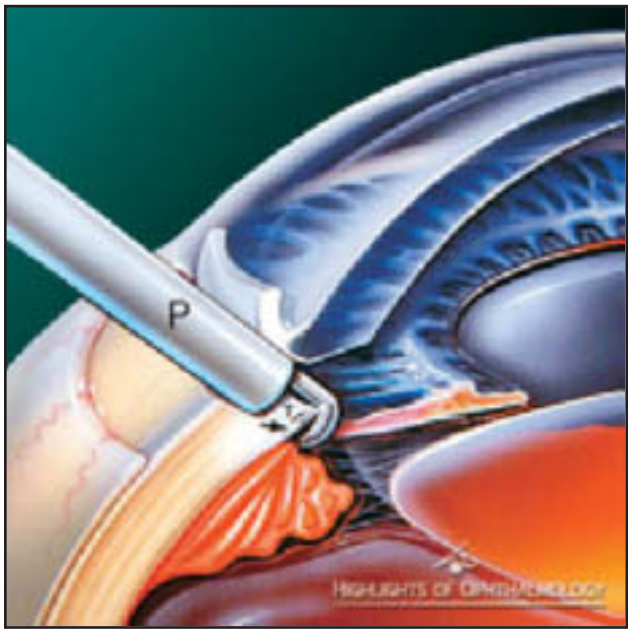


Figure 24: Modified "Tunnel" Trabeculectomy Technique - Step 4 - Trabeculectomy

The lamellar scleral flap is raised, exposing the underlying sclerocorneal bed (T). A Luntz-Dodick punch (P) is advanced to the anterior edge of the sclerocorneal bed as shown. The corneoscleral tissue (arrow) is punched out until a 2 x 2 trabeculectomy opening is made.

punched out until a 2 x 2 mm trabeculectomy opening is fashioned (Fig. 25, 26). An iridectomy is then performed, ensuring that the base of the iridectomy is wider than the trabeculectomy opening (Fig. 25, 26).

Suturing the Lamellar Scleral Flap (suggested magnification 5x)

The lamellar scleral flap is sutured with two releasable 10-0 nylon interrupted sutures, following the technique described by **Allan Kolker, M.D.** (Fig. 26). See description of this technique in Chapter titled "Enhancing the Rate of Successful Filtration" (Chapter 29).



Figure 25: Modified "Tunnel" Trabeculectomy Technique - Final Configuration

This figure shows a cross section of the final trabeculectomy configuration. Note fornix-based scleral flap sclerocorneal bed (B), scleral flap (A), and trabeculectomy opening (T).

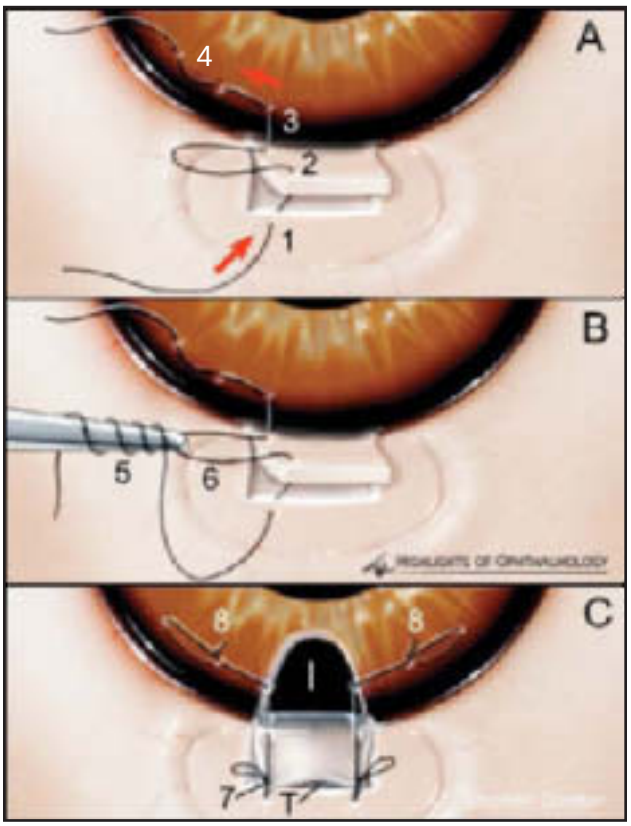


Figure 26: Modified "Tunnel" Trabeculectomy Technique - Suturing Technique

The lamellar scleral flap is sutured with two or more releasable 10-0 nylon interrupted sutures. (A) A scleral bite is taken in the posterior lip of the trabeculectomy scleral incision at the junction of the outer and middle third of the incision (1). Next, the needle is passed through the posterior corner of the lamellar scleral flap (2). Then a bite is taken at the base of the cornea into corneal tissue (3) and then another bite in the cornea (4), parallel to the limbus. (B) To tie, the posterior end of the suture is grasped with tying forceps and three throws made (5). The suture portion at the base of the cornea is grasped and pulled through the three loops (6), forming a bow-tie suture. (C) This knot is tightened onto the posterior lip of the scleral flap (7). When this configuration is tied tightly on both sides of the scleral flap, a central tunnel (T) is formed. The suture ends on the cornea are trimmed (8). The conjunctival flap is then sutured to the sclera at the limbus with a continuous 10-0 nylon suture (not shown).

Results

The procedure has been performed in 56 eyes with open angle glaucoma, followed for one to three years (average 28.4 months). Preoperative IOP ranged from 20 to 42 mm Hg (average 35 mm Hg). Postoperative IOP ranged from 10 to 18 mm Hg (average 14.6 mm Hg). Complications have been minimal, consisting of transient hyphema in eight eyes, flat chamber in four eyes (all resolved). Persistent hypotony occurred in two eyes, but both obtained good vision.

Mitomycin C was used transconjunctivally in all eyes in a titrated method using a 0.4% solution from 2 to 4 minutes, depending on the need. These results compare very favorably with results of the standard trabeculectomy technique. The results from the first 19 patients were published in J. Cataract and Refractive Surg., Vol. 20, pp. 350-352, May 1994; Maurice H. Luntz and Abraham Schlossman.

Conclusion

The tunnel scleral incision trabeculectomy technique simplifies the operation, results in smoother surgical surfaces, and gives comparable results to the standard trabeculectomy technique.

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Chapter 19
THE USE OF ANTIMETABOLITES

Benjamin F. Boyd, M.D., F.A.C.S.
Maurice Luntz, M.D., F.A.C.S.

The two main drugs of real significance to enhance surgical success following trabeculectomy are: 1) **5-Fluorouracil (5-FU)** which may be administered by subconjunctival injection during the immediate postoperative period or intraoperatively as a single application at the site of the scleral flap; and 2) **Mitomycin** which is administered with a single application applied with a sponge to the scleral bed of the already dissected trabeculectomy flap or over the area of full thickness sclera beneath the conjunctival flap, before dissection of the scleral flap or transconjunctivally before dissecting the conjunctival flap. Techniques vary with different surgeons, as well as the drug concentration used. This is because these antimetabolites or antiscarring agents are relatively new developments in glaucoma surgery and no one knows yet what is the best method and drug concentration to use.

At present, the advent and successful use of **5-FU and mitomycin are considered to be the most significant advances in glaucoma surgery of the last decade**, essentially because they are the first clinically useful anti- scarring medications in the treatment of glaucoma.

Excessive Scarring During Postoperative Period

Even if the operation is done perfectly, we have a group of variables of **postoperative wound healing**. We do not know why excessive scarring occurs in some patients (Figs. 1 and 2). On gonioscopic examination, most filtering sites show a patent internal sclerostomy after trabeculectomy

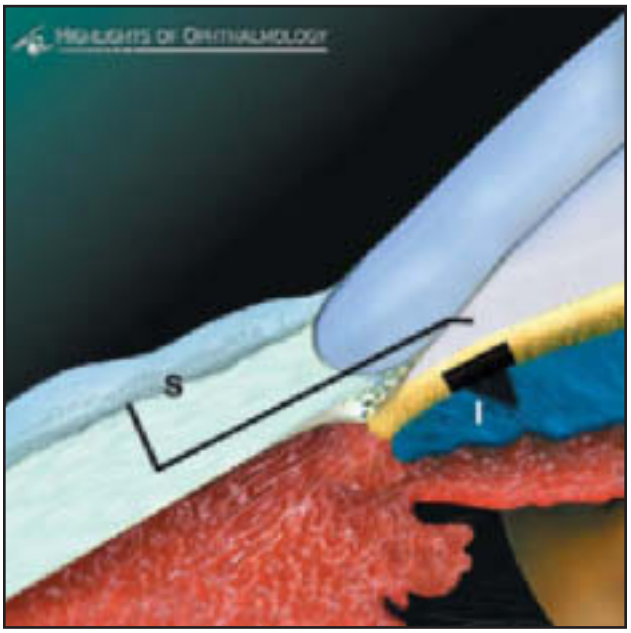


Fig. 1 : Excessive Scarring During Postoperative Wound Healing Leading to Poor Prognosis

The formation of scar tissue (S) is shown between episclera and conjunctiva. This closes the bleb causing failure of the filtration surgery. Iridectomy (I). Internal sclerostomy shown as a black square next to (I).

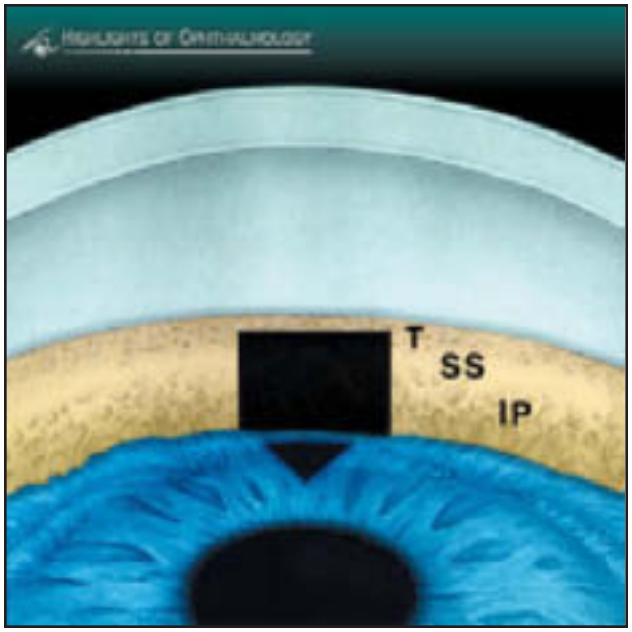


Fig. 2: Postoperative Gonioscopic View Showing Patent Internal Sclerostomy After Trabeculectomy

A gonioscopic view allows visualization of the trabecular meshwork (T), scleral spur (SS), and iris processes (IP) as well as the patent internal sclerostomy and iridectomy. Filtering operations do not heal from the inside out.

(Fig. 2). Scarring begins at the episcleral surface and proceeds to seal down the trabeculectomy flap externally (Fig. 1). Filtering operations do not heal from the inside out. The problem is not in maintaining an opening in the sclera, but with subsequent scarring at the episcleral/subconjunctival interface. Thus, external scarring seems to give some patients a poor prognosis after surgery. **It is in this group of patients that the antimetabolites are specifically recommended**.

Preoperative Conditions Contributing to Failure

Patients for whom filtration surgery is likely to fail and who therefore are specific candidates for the use of antimetabolites, can generally be divided into four groups with the following preoperative variables as outlined by **Parrish**[1]: The first group, which is becoming increasingly large, includes patients with aphakic or pseudo-phakic eyes. It is not known why aphakic or pseudophakic eyes make it more difficult to achieve successful filtration, but clearly they do. A second important variable is relative youth. For patients less than 50 years of age who are also aphakic or pseudophakic, the success rate is only one in twenty, according to the studies of **Gressel**, **Heuer** and **Parrish**[2]. The third group includes patients who have had unsuccessful filtration surgery in the past. If a first filtration procedure has failed, we know the likelihood that a second filtration operation will fail is higher than usual. The fourth group includes patients with neovascular glaucoma, irrespective of the etiology of the neovascularization (diabetic or central retinal vein occlusion).

Another major preoperative cause of failure is the race of the patient. Black patients tend to scar more actively and aggressively than Caucasians, and they have a higher failure rate. Another cause of failure is scarring of the conjunctiva from previous surgery, particularly previous filter surgery. In all these situations, the use of antimetabolites has greatly improved the success rate.

Intraoperative Variables Contributing to Failure

In addition to the preoperative variables that determine a higher likelihood of failure in the four high-risk groups just described, there are intraoperative variables, such as when an inadequate sclerectomy is created, or the iris incarcerates into the wound, or vitreous is present in the filtration surgery site.

In cases with previous cataract surgery, if we do not dissect the conjunctiva far enough forward when performing the filtration operation, the entry into the anterior chamber may be placed over the ciliary body and cause excessive bleeding. All these events are more likely to occur in the high-risk groups.

Richard Parrish, M.D., Chief of Glaucoma Service at Bascom Palmer Eye Institute in Miami, Florida and a group of ophthalmologists at the Bascom Palmer Eye Institute pioneered the use of antimetabolites, specifically 5-fluorouracil (5-FU) and mitomycin C (MMC) in filtering surgery. Today, nine years after the introduction of mitomycin C in the United States, surgeons tend to use antimetabolites more conservatively in appreciation of the late-onset complications, such as thin walled blebs that may predispose to the development of bleb leaks, endophthalmitis, and hypotony maculopathy.

It is important to put into historical perspective the problems that ophthalmologists are seeing today after filtering surgery with mitomycin C. He quotes from the text, «Sclero-corneal Trephining in the Operative Treatment of Glaucoma,» written in 1914 by Colonel Robert Henry Elliot, which describes an uneventful glaucoma surgery, trephination, followed by a late-onset bacterial conjunctivitis and subsequent endophthalmitis. Thirty-six years later in 1958, Dr. Saul Sugar, one of the great international deans of glaucoma surgery, concluded in an article «Late infection of filtering conjunctival scars,» that although trephination had the advantage of greater intraocular pressure lowering compared to iridencleisis, it was negated by a higher incidence of bleb infection. Looking back at the conclusions of Elliott and Sugar leads Parrish to the realization that late-onset infections after filtering surgery are not manifestations of a new problem, but the resurgence of an old problem. Today ophthalmologists are reevaluating how antimetabolites should be used. **Dr. Philip Chen**, formerly a glaucoma fellow at the Bascom Palmer Eye Institute, and now an Assistant Professor at the University of Washington, conducted a survey of antimetabolite use among members of the American and Japanese Glaucoma Societies. He determined that surgeons now tend to use a slightly lower concentration of mitomycin C for a shorter duration than initially described. The concentration of mitomycin C now used most frequently is 0.4 mg/ml for 3 to 4 minutes rather than 0.5 mg/ml for 5 minutes, as originally suggested by Dr. David Palmer, who introduced the use of mitomycin C to American ophthalmologists.

Many variables in the application of antimetabolites cannot be determined simply by assessing the concentration and the length of exposure. How the antimetabolite is applied and later removed may influence the drug concentration and the ultimate clinical outcome.

Use of 5-Fluorouracil

In the last five years surgeons have moved toward the use of intraoperative 5-FU in a manner similar to that used for mitomycin C. (**Editor's Note**: Many surgeons use 5-FU in patients with low to moderate risk and Mitomycin in high risk eyes.) Commercially 5-FU (Adrucil) is available at a concentration 50 mg/ml. Undiluted 5-FU is usually applied on a cellulose cell or sponge fragment to the episcleral surface over the area of the planned trabeculectomy directly beneath and in contact with the conjunctival flap. Some surgeons outline the trabeculectomy flap and then apply the sponge to the scleral surface. If the sponge soaked with either mitomycin C or 5-FU is placed on the sclera and the conjunctiva is pulled superiorly and posteriorly against the globe, additional fluid with the antimetabolite is squeezed from the sponge. **Parrish** prefers to dry the episcleral surface with a dry cellulose sponge to quickly absorb as much of the antimetabolite from the surgical field after application, prior to irrigation with 10 ml sterile saline solution. Other surgeons simply irrigate the area copiously.

Use of Mitomycin C

The use of intraoperative mitomycin C in eyes with good prognosis is decreasing. Patients less than 50 years old and African Americans are more likely to be treated with intraoperative mitomycin C than 5-FU. A key to surgical success to prevent immediate postoperative hypotony with mitomycin C is to ensure that the flap is tightly sutured. Placing sufficiently tight sutures that can be either cut with an argon laser or released sequentially helps minimize immediate postoperative hypotony. If only two sutures are placed in the scleral flap and the intraocular pressure remains elevated after cutting or releasing the first suture, the risk of hypotony is substantial when the only remaining suture is cut. Placing three or four 10-0 nylon sutures and cutting them sequentially minimizes the risk of this development. The effects of mitomycin C on delaying wound healing are prolonged and sutures may be cut or released up to one month after trabeculectomy and still result in profound intraocular pressure lowering.

Drainage Implant Surgery versus Standard Limbal Trabeculectomy

Parrish is now seeking to determine the best treatment for eyes with glaucoma that have a worse than usual prognosis, such as after failed trabeculectomy or previous cataract surgery. He, **Dr. Steven Gedde** of the Bascom Palmer Eye Institute, and **Dr. Dale Heuer**, Chairman of Ophthalmology, Medical College of Wisconsin, have designed a clinical trial, the TVT (tube versus trabeculectomy) that will compare the safety and effectiveness of drainage implant surgery using a 350 mm Baerveldt implant (Pharmacia) to a standard limbal trabeculectomy with antimetabolites. Patients with poor prognosis are now being randomly assigned to one of these two surgical treatments at 13 clinical centers.

Many ophthalmologists believe that the risk of late bleb or intraocular infections associated with drainage implants is substantially less than with trabeculectomy and mitomycin C. Intraocular pressures in the very high range, such as 30 - 40 mmHg, are less likely to be lowered immediately after drainage implant surgery than with a trabeculectomy with antimetabolite. The most efficient and ethical way to sort out the benefits and risks of these two treatments is to conduct a clinical trial. The study will determine which of these two techniques will provide the most effective and safest method of lowering intraocular pressure. Independent funding to support this trial is being provided by Pharmacia.

Indications for Antimetabolites

The main and specific indications for the use of antimetabolites are: 5-FU in the low to moderate and intermediate risk patients and mitomycin in the high risk groups, because of its toxicity. An increasing number of surgeons, however, are using mitomycin routinely in lower concentrations. 5-FU is being used more regularly by subconjunctival injection postoperatively in routine cases that present early signs of possible bleb failure. 5-FU can be used in a single application intraoperatively and is somewhat less toxic than mitomycin, but not as effective.

THE USE OF 5-FU

Subconjunctival Administration Postoperatively

5-FU is usually given postoperatively at the first sign of vascular ingrowth into the bleb, thickening of the bleb or increasing intraocular pressure in the early postoperative period. Characteristically on the second or third postoperative day, after allowing the wound to heal 2 or 3 days

following surgery. Delayed administration of 5-FU has allowed him to avoid most wound leaks. If the delay is only 2 or 3 days, scarring of the bleb does not usually have time to occur.

At the first signs of vascular ingrowth and thickening of the bleb, Simmons injects it daily, hopefully until the scarring reverses or the patient can not tolerate further administration.

The dosage for each injection is 5 mg (0.1 cc or ml). The vial usually contains 10cc. The cost is about US$8.00 per vial. It is very important to inject 5-FU at the slit lamp. Proparacaine anesthesia and a drop of phenylephrine will vasoconstrict the vessels and decrease the incidence of bleeding, which can otherwise be a problem. The injection is given subconjunctivally into the fornix in the periphery of the bulbar conjunctiva. Injecting too close to the bleb can create a leak merely from the passage of the needle into the filtering tissues. These injections are continued daily until toxicity develops or until the fibrosis of the bleb ceases and a good functional bleb is established.

Tolerability of 5-FU

Tolerability is an important limitation of 5-FU. Some extremely sensitive patients develop irritation and discomfort after the first two or three injections, and others tolerate 20 or 25 injections before they show any signs of toxicity. On the average, a patient will exhibit toxicity after seven or eight injections of 5-FU. The important toxicity occurs in the epithelium of the cornea. 5-FU seems to inhibit the proliferation of stem cells that regenerate the epithelium of the cornea in the limbal region. In patients who manifest this effect, the epithelium becomes thin, then stippled and often totally absent. Upon cessation of 5-FU administration the epithelial cells will begin to grow again, usually after 14 to 20 days. Subsequent to the last injection the epithelium will regenerate essentially in all cases. Absence of the epithelium yields an unpleasant foreign body sensation and also causes reflex congestion of the conjunctiva.

Stamper points out that any time that you have something that makes your therapy more effective, you cannot expect to get away without some problems.[3] And 5-Fluorouracil is no exception. The problems that are most frequently encountered with 5-Fluorouracil are related to the very things that we want 5-Fluorouracil to do. We want it to prevent or slow down the scarring-healing. Unfortunately, 5-Fluorouracil does not discriminate. So it does not discriminate between a fibroblast, which is our enemy, and a conjunctival or corneal epithelial cell which is our friend. With 5-Fluorouracil, the division of the new corneal epithelial cells is going to be inhibited. So, you get wound leaks and corneal toxicity that ranges anywhere from punctate keratopathy to frank corneal abrasions . Those are the most common.

Use of Bandage Contact Lens to Increase Tolerability

A large bandage contact lens will minimize 5-FU's side effects and greatly improve the patient's tolerance of 5-FU administration. The bandage contact lens, which covers the cornea, reduces the foreign body sensation and the reflex congestion of the eye due to the epithelial defect . It therefore allows prolonged administration of 5-FU, usually until the patient no longer needs it and bleb scarring has ceased.

A bleb leak following 5-FU injections is treated with a large bandage contact lens (22 mm diameter) which extends into the periphery of the fornix covering the wound itself . This allows the conjunctival wound to be supported and a good filtration bleb that retains fluid to be developed. Eventually, when the 5-FU injections cease, the cornea has cleared, the epithelium has regenerated, and the wound has healed, he removes the bandage contact lens.

On the other hand, if in spite of these therapeutic measures the patient is in pain, the cornea is getting hazier, or the wound is breaking down, you quit. But if none of these occurs and the scarring process is decreasing, the bleb is getting better and the eye is quiet, you might continue 5-FU administration until your clinical judgment leads you to stop.

Most surgeons limit 5-FU to 10 injections of 5mg each, a total of 50mg. If the cornea remains unaffected, a higher dose of 5-FU can be given.

Wound Leaks

Another side effect is that in some patients the wound, which originally was sealed and appeared healed, begins to leak at approximately 5-10 days after initiation of 5-FU therapy. This can occur with limbal based or fornix based conjunctival flaps, but is more common in the latter.

Meticulous closure of the conjunctiva is very helpful to prevent conjunctival wound leaks. Stamper[3] personally uses an atraumatic needle (Fig. 3) and tries to make the incision in the conjunctiva fairly far from the limbus so that the aqueous drainage is as far away from the conjunctival incision as possible. He closes the conjunctiva with a running 11-0 Mersilene suture on an atraumatic, non-cutting needle, so that the needle does not cut any bigger hole in the conjunctiva than absolutely necessary (Fig. 3). It is impressive sometimes to see leaks coming out of the suture tracks, even when you use such fine sutures as 10-0 and 11-0. We really have to handle conjunctiva more delicately than we have in the past.

Results With 5-FU

With the method and precautions described, in those cases of eyes that have not had previous surgery one expects 75 to 80% success rate without 5-FU but with 5-Fluorouracil the success rate is into the 90% range.

Luntz has observed that the effect of antimetabolites used with filtration surgery lead to an additional drop in the intraocular pressure of approximately 20%. The main benefit from antimetabolites, however, is that they significantly increase the number of blebs that filter.

Rationale for Using 5-FU

The rationale for using 5-FU is that it interferes with the synthesis of both DNA and RNA. In rapidly growing fibroblasts, as in rapidly growing tumor cells, if the replication of DNA can be stopped, we can halt or substantially diminish the proliferation of the cell. Since the fibroblast is the primary culprit in filtering-surgery failure (Fig. 1), slowing its growth increases the success of filtration surgery.

Dr. Peng T. Khaw's laboratory research at the Institute of Ophthalmology in London has helped

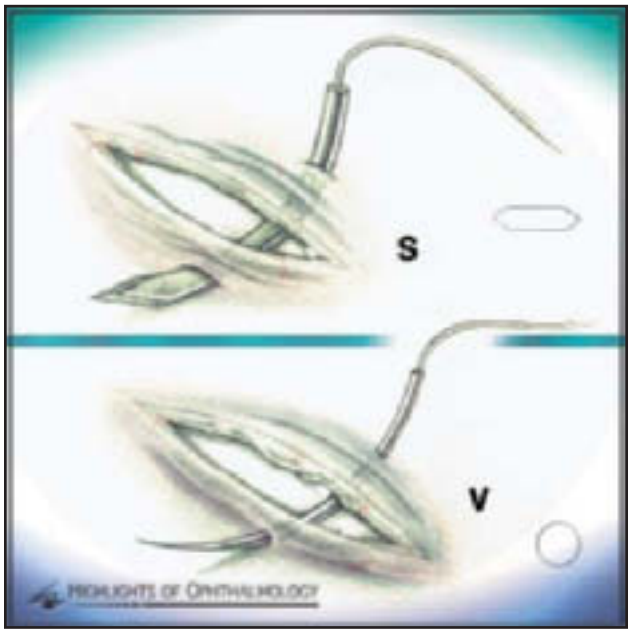
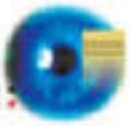


Fig. 3: Minimizing Wound Leaks When Using Antimetabolites

Tight wound closure is essential for conjunctival healing. The top diagram illustrates how the spatula needle (S) creates a wide slit in the conjunctiva which allows wound leakage because the suture does not fill the hole created by the needle. A cross section of the needle is shown adjacent to the view of the entire needle. The lower diagram shows how a vascular-taper needle (V) minimizes wound leakage. The diameter of the needle and the diameter of the suture are nearly the same which allows for tight wound closure. This needle is round in cross section.



us understand how the short dose treatments of antimetabolites are working and how we can further refine them in the future.(4) We know that the area, degree and length of fibroblast inhibition can be controlled by varying the concentration or type of agent, and potentially this may enable us to control bleb position, thickness and possibly even titrate the final intraocular pressure.

When to Use 5-FU and When Mitomycin

5-FU is indicated in a single application as previously described or by subconjunctival injection postoperatively in patients with low or moderate risk factors, including patients under 40, Afro-Caribbeans and those who have been using topical medications for more than one year, especially pilocarpine or adrenaline. It may also be considered useful in patients with intermediate risk factors such as previous conjunctival surgery including trabeculectomy and cataract surgery. When used as described, it has lowered failure rate to less than half the former levels.

Mitomycin, on the other hand, is a more potent and toxic drug, leading to avascular and cystic blebs which may result in a high incidence of leaks and endophthalmitis in the future. It is indicated in eyes which have failed with a previous trabeculectomy with 5-FU, glaucoma with uveitis, glaucoma with chronic conjunctival inflammation, aphakia and multiple risk factors.

The use of mitomycin and 5-FU in filtering glaucoma surgery is one of the most important developments in many years since it has been demonstrated that the lower the final intraocular pressure after surgery the better the visual prognosis. The main reason for surgical failure and suboptimal lowering of intraocular pressure is the scarring response after glaucoma filtration surgery. The use of the antimetabolites has considerably reduced the failure rate and also results in a lower final intraocular pressure.

THE USE OF MITOMYCIN

There is some controversy about how mitomycin acts. Although some investigators feel that it is cidal to the fibroblast, there is some recent tissue culture work which suggests that, while the fibroblasts are inhibited from replicating for four to six weeks, they are still viable after the application of mitomycin. Simmons considers that this recent work is very significant because it suggests that mitomycin is just what we want in terms of a fibroblast inhibitor. It also explains the very promising results obtained up to this point. An important concern is the long term effect of this drug on these blebs. Some of them become quite thin and avascular causing concern about the potential long-term risk of breakdown and infection leading to endophthalmitis. The risk of endophthalmitis has motivated many surgeons to return to use of a single dose intraoperative of 5-FU. (See technique of Dr. Peng Khaw earlier in this chapter).

Method of Application of Mitomycin

The drug comes as a powder that is dissolved for use. Because it forms a very powerful and toxic drug, the physician or nurse preparing it must protect his/her own tissues with gloves, goggles, and a splash-proof bottle cap (cytotoxic handling code). Soaking towels are incinerated.

Some surgeons are using mitomycin routinely but in lower concentrations. **Caldwell** uses it routinely in trabeculectomies as described by **Palmer** with excellent results. A solution of 0.2 mg/ml mitomycin is prepared by mixing the contents of a 5-mg vial of mitomycin into 25 ml of sterile water; a Weck cell sponge is soaked in the mitomycin and applied directly to the scleral flap for approximately 4 minutes.[7] (See also transconjunctival technique later in this Chapter - **Editor**.)

Arenas (see Chapter 21) has recently modified his trabeculectomy ab-externo with the incorporation of a diamond drill to facilitate the opening of the external wall of Schlemm's canal and allow him to use mitomycin routinely in trabeculectomy ab-externo applying a sponge with very diluted doses of the drug (0.04 mg per ml, one tenth the standard dose of 0.4 mg per ml). Before the drill was used, the external layer of Schlemm's canal had to be penetrated with a knife, which could cause some difficulties. The first step in this easy new technique is to discover Schlemm's canal. Dissection with the knife is stopped as soon as some fluid is reached, and drilling begins. The diamond drill, which is 0.1 mm in diameter and moves relatively slowly at about 6,000 revolutions per minute, allows us to open the external walls of the trabeculum very slowly. The drill is moved side to side in the trabeculum area until we get enough leaking of aqueous. The slow movement of the drill almost guarantees that we will not perforate the anterior chamber.

Arenas uses this technique with simple application of very diluted doses of mitomycin in all his cases, provided he does not enter the anterior chamber. There is no risk of damaging the corneal endothelium or any other structure of the eye if the anterior chamber is not entered. It is important, however, that he does use a much weaker dose of mitomycin as outlined above. **Arenas**[16] has used mitomycin routinely on 72 cases of trabeculectomy ab-externo and has had no flat chambers or other complications to date.

Some surgeons put the mitomycin underneath the scleral flap. No one really knows at this time which is the better method.(Fig. 4).

Some surgeons apply the mitomycin on the episclera before dissecting the outer trabeculectomy scleral flap. Others prefer to dissect the scleral flap

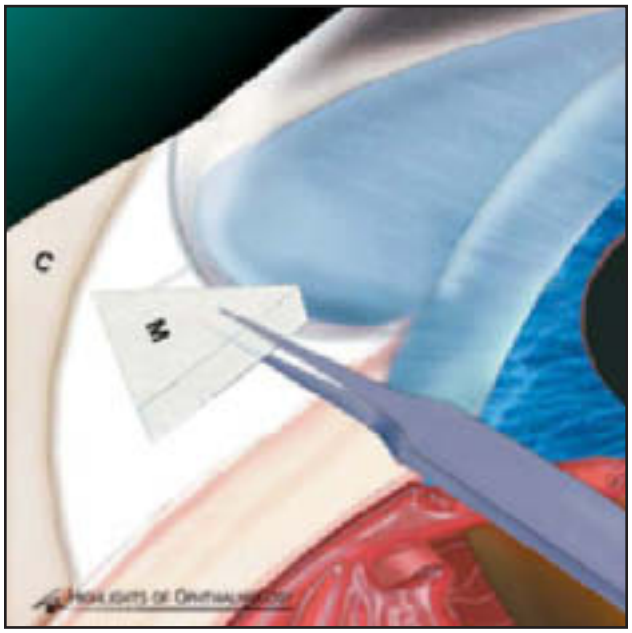


Fig. 4: Mitomycin Soaked Sponge Placed Directly over Sclera

The cellulose sponge soaked with a 0.4 mg per cc dilution of mitomycin (M) is placed during four minutes directly on top of the sclera in the area where the scleral flap will be dissected. Some surgeons prefer to apply the mitomycin over the scleral bed of the trabeculectomy, underneath the scleral flap but these constitute a minority. Do not enter the eye prior to the application of the mitomycin. Fornix based conjunctival flap (C).

and apply the sponge on the scleral bed of the trabeculectomy flap. (**Editor's Note**: This is not a popular method because the Mitomycin in this location damages the scleral flap and scleral bed). It is most important not to enter the eye prior to the application of mitomycin because this drug is very powerful and if a leak occurs it can cause extensive intraocular damage.

It is important not to expose the cut back edge of the conjunctival flap to the sponge. This helps conjunctival wound closure without leaks.

Mitomycin blebs seem to fall into two groups. The first group looks rather like a 5-Fluorouracil filter with a very diffuse pale and thin but not avascular bleb. These occur about half the time. The other half of the blebs are thin, clear, white and sharply demarcated. Why the bleb tissue does not become re-vascularized or scars as it would if killed by some other agents such as cautery or alcohol, nobody knows for certain. The recent tissue culture work suggesting continued viability of fibroblasts may explain this.

Luntz[5] titrates the dosage of mitomycin applied at the time of filtration surgery to minimize the risk of complications. The titration is achieved as follows:

1) A standard 0.4% solution is used.

2) If the lowest titration is required, the mitomycin is applied to the conjunctiva via a soaked Weck cell sponge for 3-4 minutes, depending on the dosage the surgeon selects. Then the sponge is carefully removed, and the area of the surgery treated with mitomycin is profusely irrigated with balanced salt or saline solution.

3) If a higher dose is required, four minutes of mitomycin are applied to the conjunctiva, and, following a peritomy, mitomycin is applied under the conjunctiva for 1-3 minutes. Again the area of the surgery treated with mitomycin is profusely irrigated with balanced salt or saline solution. (Fig. 5).

The dosage applied will depend on the degree of scarring in the conjunctiva and whether the patient is Caucasian or pigmented. In lightly scarred conjunctivae in the Caucasian patient, the transconjunctival application is used for 3-4 minutes. In more

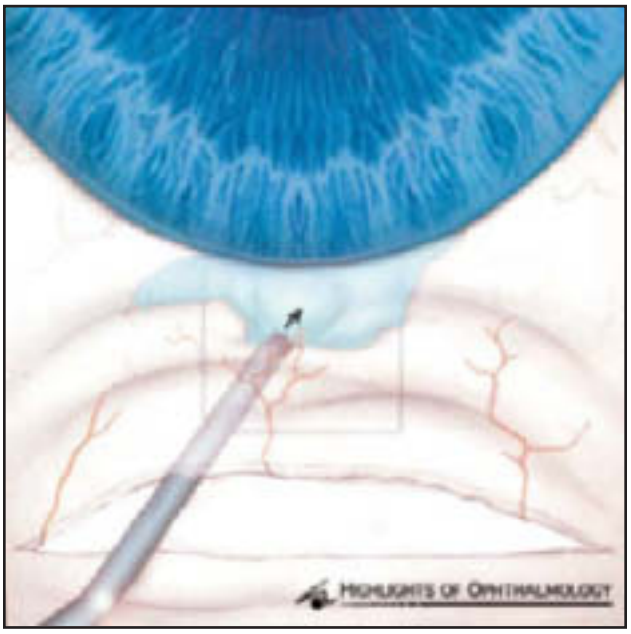


Fig. 5: Profuse Irrigation After Removal of Mitomycin Sponge

After the cellulose sponge is removed, the area of the surgery treated with mitomycin is profusely irrigated with balanced salt or saline solution. It is very important that all the antimetabolite be irrigated from the field. When using mitomycin, a larger amount of irrigating fluid is used than when using a single application of 5-FU. Mitomycin is much more toxic.

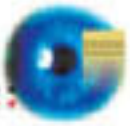
heavily scarred conjunctiva from previous surgery in a Caucasian patient, one would use four minutes applied to the conjunctiva and 1-2 minutes applied under the conjunctiva. In pigmented patients or Caucasian patients under 40 years of age, in uveitis, for the initial surgery, one would use four minutes of mitomycin applied to the conjunctiva. In pigmented patients who have had previous surgery with moderate scarring, one would use four minutes of application on the conjunctiva and 1-2 minutes under the conjunctiva. In pigmented patients with previous surgery and a heavily scarred conjunctiva, one would use the full dosage of four minutes applied on the conjunctiva and three minutes applied under the conjunctiva. The titration of the dosage of mitomycin is an individual assessment, as no good studies have standardized the method of application and the dosage of mitomycin relative to the degree of conjunctival scarring. Each surgeon needs to apply his/her own judgment in terms of dosage to each individual case.

Transconjunctival Application

A 0.4% solution of mitomycin is drawn into a tuberculin syringe up to the 2cc mark. The syringe is emptied into a glass dish. Three or four Weck cell sponges are cut across the tip of the sponge (leaving a rectangular-shaped sponge). These sponges are then soaked in the mitomycin in the Petrie dish. The patient's conjunctiva is evaluated and the site for the surgery selected. One Weck cell sponge is then applied to the site for one minute, discarded, and the second Weck cell sponge applied for one minute, etc., for 3-4 minutes, depending on the dosage that the surgeon has selected for that patient. Up to four minutes of transconjunctival application can be used.

Subconjunctival Application

In this case, the surgeon has decided on a higher dosage than four minutes of transconjunctival application. Following four minutes of transconjunctival application, the mitomycin is thoroughly washed from the conjunctival surface with balanced salt solution. A peritomy is performed at the site of the surgery, forming a fornix-based flap which is then dissected from the sclera to form a subconjunctival pocket. Taking a Weck cell sponge, four small pieces of sponge are cut and soaked in the mitomycin solution. Each of these four small sponges soaked with mitomycin is placed under the conjunctiva for one minute. Depending on the dosage that the surgeon has selected, two, three or four of these sponges are used, giving a dose of two, three or four minutes of exposure to the mitomycin. Following this procedure, the mitomycin is thoroughly washed from the subconjunctival space with balanced salt solution (Fig. 5). The surgeon selects a minimal dose of mitomycin that he/she considers adequate for each individual case, and, in this way, attempts to minimize the postoperative complications from mitomycin.



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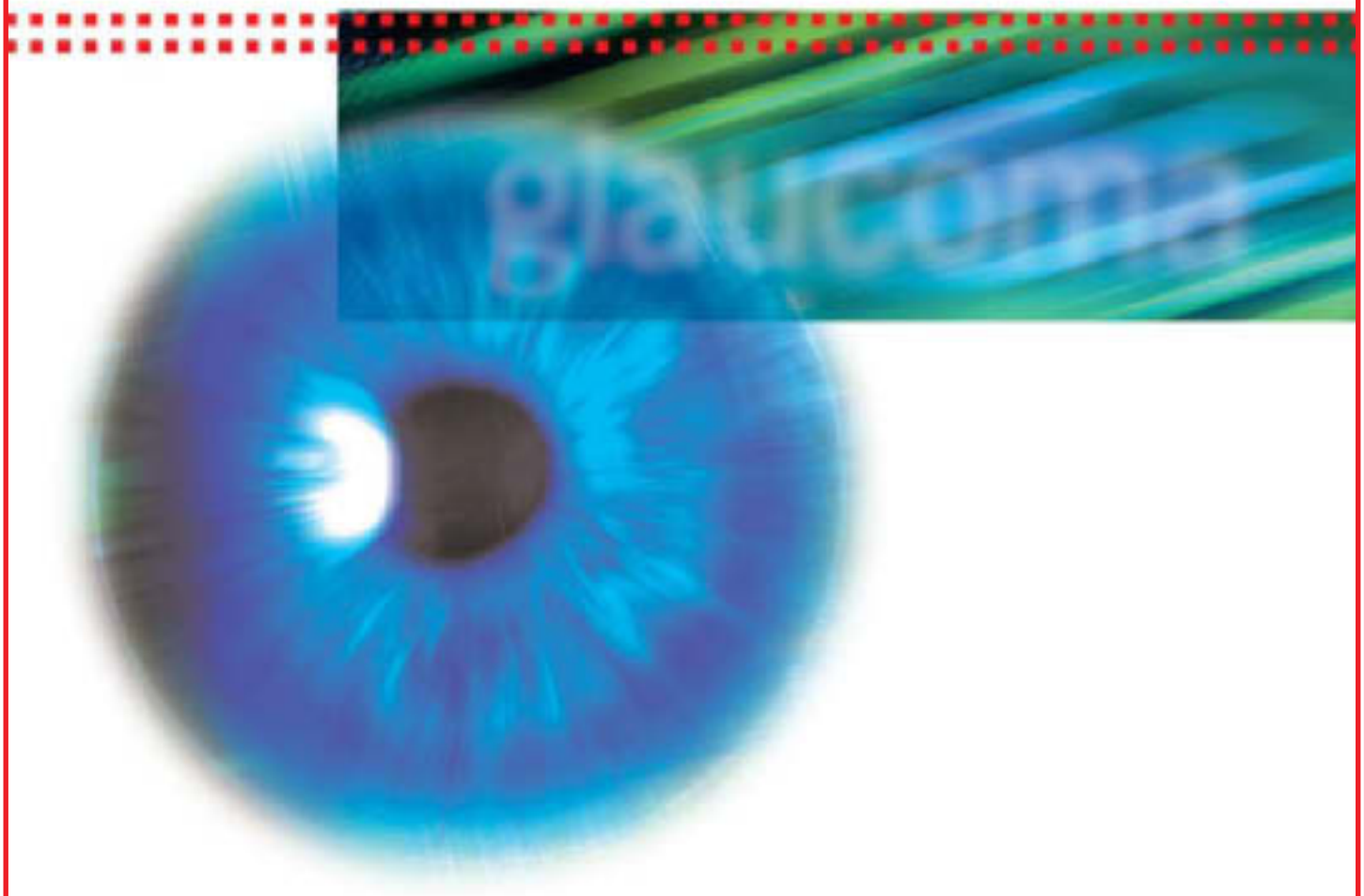
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Incisional Surgical Management

B - The Non-Penetrating Filtering Operations



Chapter 20
OVERVIEW - CONTROVERSIES – SIMILARITIES AND DIFFERENCES

Benjamin F. Boyd, M.D., F.A.C.S.
Maurice Luntz, M.D., F.A.C.S.

Heated Debate

In the past three years, there have been strong debates centered on whether non-penetrating filtering surgical procedures for open angle glaucoma have real merits as compared with trabeculectomy protected by a scleral flap with or without antimetabolites, with or without releasable sutures. In some instances, these debates have become quite heated.

Surgeons in the United States in particular, tend to be more conservative for good reasons related to the established standards of care in the communities where they practice. They are not convinced that the non-penetrating filtering procedures in cases of open angle glaucoma are as effective as their procedure of choice: the guarded, not full thickness, trabeculectomy with or without antimetabolites which has a proven effectiveness (Chapters 18 - 19). This is especially pertinent in the United States where patients are now operated only after medical therapy and laser trabeculoplasty have failed to control intraocular pressure, treatments which, if long standing, may adversely affect the results of surgery compared to the use of surgery as the primary treatment.

Surgeons in some other parts of the world continue the search for surgical procedures that will be effective and safe in their patients as primary care with minimal complications to be used instead of medical therapy. Within this category are the non-penetrating filtering operations that we are presenting in this volume, Chapters 20-27.

(**Editor's Note**: the pioneers and strong advocates of this group of operations are all distinguished and prestigious surgeons from outside the U.S., essentially Europe and Latin America.)

Lack of Need for Debate

In reality, there is no need for heated debates. Those of us who have managed many patients suffering from open angle glaucoma are fully aware that this is not a disease that has one best solution for all patients in all communities. It is not like cataract surgery in which, after years of experience and technological advance, most ophthalmic surgeons agree that phacoemulsification is the best procedure for the patient in spite of the difficulties existing with this operation, such as costs and the complex transition from extracapsular to phacoemulsification. But this can be overcome with training. In phacoemulsification, the differences now existing are just variations by different prestigious surgeons who make a slight modification or sometimes create important changes in surgical principles (such as cracking vs chopping). But the truth is quite evident to all:

phaco is the best but we can not always perform phaco, even though it is the procedure of choice in cataract surgery. Why not? Simply because in many communities socioeconomic and cultural factors do not make the performance of this operation feasible in most patients.

On the other hand, when we deal with glaucoma, it is quite evident that management of this disease needs a **multi factorial solution**. There is neither one medication nor one surgical procedure that is going to be the best for all patients throughout the world. The ophthalmologist's responsibility is to analyze and study which of the different methods of treatment, both medical and surgical, serves his/her patients best according to the personal and professional resources that the patient and the physician have in providing the most advanced medical care appropriate and feasible in their community.

The Significant Advances in Medical Therapy - Limitations

There is absolutely no question that industry has made remarkable efforts to provide us with medications that are much more efficacious than what we had available even three or five years ago. The major players in ophthalmic industry have made a significant investment in financial resources and scientific personnel to provide us, and through us, to millions of patients throughout the world, extremely useful, effective and simple to use medications.

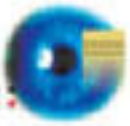
But we all know medical therapy in glaucoma has its limitations. One of them, perhaps the main one, is the patients' lack of compliance. Levels of education have a great deal to do with the patient complying with his/her responsibility to follow the medical treatment that the physician has recommended. In addition, in communities where ophthalmological services and resources are limited, the availability to patients of these medications is also limited.

What is Best for Patients in Different Parts of the World

When it becomes necessary to operate, the experience with trabeculectomies with a scleral flap with or without the use of low concentrations of antimetabolites and releasable sutures when indicated, is quite good. The incidence of flat anterior chambers in these procedures at present is less than 1.5 to 2%. Other complications such as infection, are also very limited.

Up to a few years ago, a major problem had been the exaggerated blebs that formed as a result of utilizing doses of antimetabolites that are unnecessarily strong. We know now that antimetabolites may be very useful but should be used in lower concentrations. On the other hand, the non-penetrating filtering operations that we present here may be of great use for other types of societies, precisely those societies where physicians are looking for control of intraocular pressure with a primary surgical procedure. It also depends on the goals of the physician. If the aim is to end with a low intraocular pressure such as below 10, there is no question that trabeculectomies combined with antimetabolites and releasable sutures will attain this aim much more effectively than the non-penetrating filtering operations. The latter have proven to have a good result in lowering intraocular pressure but at moderate levels of 12 to 15 mm Hg.

In essence, there are different needs in society and different aims for the physician. The surgical decisions depend on what society the physician is working in and what his/her aims are regarding the levels of intraocular pressure to be attained. There is no question that the non-penetrating filtering operations that we are presenting in Chapters 20-27 are effective. But it is not prudent nor beneficial to take sides and say which is the very best for all people. There are indications and contraindications for both groups of procedures. All of them work.



The Strong Need for Training

Even though the non-penetrating filtering operations are effective, most ophthalmologists do not have a clear concept of how they work. Most highly trained ophthalmologists do not know how to do them, not because they are surgically incompetent but because they have not had the opportunity to learn the techniques. Their proponents have a challenging task ahead to organize laboratory teaching courses at most major Congresses that would provide the opportunity to learn how to perform these techniques. In this Volume we have made significant efforts to contribute to the understanding of how these procedures work and the main differences that characterize each other.

Principles of Non-Penetrating Filtering Operations

Non-penetrating filtering operations are intended to facilitate the passage of aqueous humor through the trabeculum and Schlemm's canal bypassing the inner wall of Schlemm's canal (known as the juxta-canalicular meshwork) which is the site of highest resistance to aqueous outflow (Fig. 1). Which mechanism takes place depends on the specific technique utilized, but they are all somewhat similar in their surgical concepts.

The main principle behind nonpenetrating glaucoma surgery is to avoid opening the anterior chamber and decompressing the eye, thereby preventing most of the possible but also infrequent serious complications of standard trabeculectomy.

Anatomy and Fluid Dynamics of the Trabeculum and Schlemm's Canal

Normal vs Open Angle Glaucoma

Surgeons performing a non-penetrating filtering operation must be very familiar with the anatomy of Schlemm's canal and the fluid dynamics in the glaucomatous eye as compared with the normal eye. Between the endothelial lined Schlemm's canal and the inner tissues that lead to the anterior chamber, we find the trabecular meshwork which is a sponge like tissue. In normal eyes the aqueous humor seeps easily from the anterior chamber through this meshwork until it reaches the internal wall or floor of Schlemm's canal (SC) (Fig. 1-A). In this wall there is a single layer of very active endothelium that transports the aqueous humor through the mechanism of endocytosis. In open angle glaucoma this layer of endothelium in the inner wall of Schlemm's canal is altered and becomes the site of highest resistance to aqueous outflow. Aqueous then filters more slowly into the lumen of Schlemm's canal (SC) leading to a rise in the intraocular pressure (IOP) (Fig. 1-B). There is probably also increased resistance to flow of aqueous in the floor of Schlemm's canal (juxtacanalicular trabecular meshwork). We identify the inner wall as "the floor" of Schlemm's canal (SC). Once the aqueous humor gets into the lumen of the canal it is slowly drained through small openings located in the external wall of the (SC) identified as the "roof of Schlemm's canal" (Fig. 1-A). The real argument over the years has been whether the site of resistance is an altered trabecular meshwork or this layer of endothelium. There is evidence on both sides.

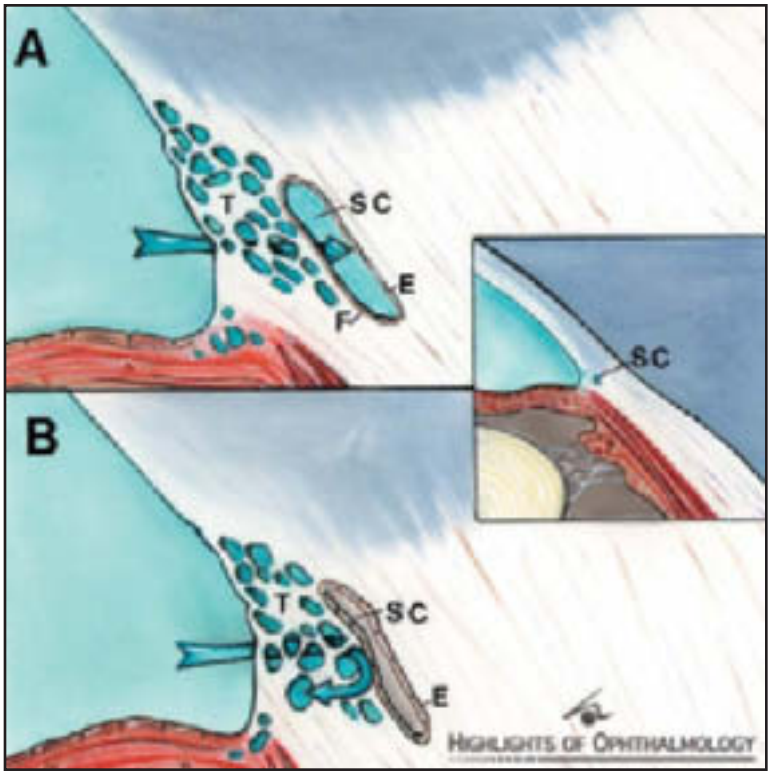


Figure 1: Normal Anatomy and Fluid Dynamics as Compared with the Anatomy and Fluid Dynamics of a Glaucoma Patient

(A) Illustrates normal flow of aqueous humor through the trabecular meshwork (T) to the floor (F) of the Schlemm's canal (SC). Active transport of the aqueous humor occurs through the normal endothelium (E) to the lumen of the canal. It is then drained through small openings in the external wall or roof of Schlemm's canal (SC), into scleral collector channels and then into capillaries and veins within the subconjunctival tissues.

(B) In a diseased eye with open angle glaucoma, the endothelium (E) of Schlemm's canal is more resistant to aqueous outflow as is the immediately adjacent trabecular meshwork. This is the site of highest resistance to aqueous flow. Passage of aqueous humor is very slow, resulting in the increased IOP of glaucoma.

(Inset) Anatomically, the Schlemm's canal (SC) is located slightly behind the limbus.

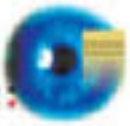
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From this point on the aqueous flows into the capillaries and veins within the subconjunctival tissues and intra-scleral channels. This continuous circulation is what maintains normal intraocular pressure.

Anatomically the (SC) is located slightly behind the limbus (Inset Fig. 1) and the clear corneal trabeculum is easy to see under a deep scleral flap.

The Four Main Techniques

At present, there are four main surgical procedures which are effective in lowering intraocular pressure medium and long term without the need to penetrate into the anterior chamber and decompressing the eye. **Eduardo Arenas, M.D.**, in Bogota, Colombia, is the pioneer of the **modern** techniques. **Arenas** developed the **Ab-Externo Trabeculectomy**



in 1984 and has extensive and highly positive experience with its results (Chapter 21). As a matter of fact, some important subsequent developments and procedures are modifications of **Arenas ab-externo trabeculectomy** as expressed by Maldonado in Chapter 25. **Arenas** ab-externo original procedures were first published in the HIGHLIGHTS in 1991, 1993 and 1996 and then in 2000 (See bibliography.)

Robert Stegmann, M.D., in South Africa, with the engineering help of **Hans Grieshaber**, first developed trabeculo-viscotomy which Stegmann later modified to the present **viscocanalostomy** (Chapter 23). Both of these techniques were also initially published in the HIGHLIGHTS in 1993 (see bibliography.) **Stegmann's** viscocanalostomy has stimulated a significant amount of interest worldwide.

Mermoud in Switzerland and other surgeons in different prestigious institutions mostly in Europe and Elie Dahan and co-authors in South Africa use a **deep sclerectomy** which, if it eventually fails, may presumably be repeated with no major consequences, as emphasized by Dahan. Mermoud modified the original deep sclerectomy by placing a collagen intrascleral implant over the filtering zone (Chapter 22.)

Arturo Maldonado-Bas,M.D., Chief of the Department of Ophthalmology in Cordoba, Argentina has recently reported (ASCRS 2000) the **excimer laser trabecular ablation (LTA)**. **Maldonado** has proven its effectiveness long term and its simplicity for surgeons who are familiar with the use of the excimer laser (Chapter 25).

Surgical Principles Common to All the Operations

All the non-penetrating filtering procedures attempt to create a very thin communication between the anterior chamber and the intrascleral channels into the episcleral and conjunctival veins without decompressing the eye. In all of them, Schlemm's canal is unroofed and its inner walls are significantly thinned out. All of them require very delicate, complex microscopic dissection and maneuvers and are more difficult to perform than classic trabeculectomy. Perhaps Arenas' ab-externo technique and Maldonado's excimer laser, true "no touch" technique are the least complex. All of them are effective and all of them have reported fewer postoperative complications than classic trabeculectomy but they are no better than the classical trabeculectomy in controlling intraocular pressure. The exception may be that Stegmann's own results with viscocanalostomy seem to show that in his hands, lowering of intraocular pressure in black and high-risk patients is better than standard trabeculectomy.

In all the non-penetrating filtering procedures for glaucoma, the surgeon first dissects the episclera and the deep sclera and dissects down to reach the roof of Schlemm’s canal (external wall) by different surgical means (Fig. 1-A). The altered endothelium of Schlemm's canal is removed, portions of the trabeculum are ablated, Schlemm's canal is "unroofed" whereby its external wall is removed with further dissection. These techniques effectively bypass the barriers created by the "sick" endothelium of Schlemm's canal (Fig. 1-B).

Arenas believes that by achieving continuous micro filtration with a very low rate of aqueous drainage, a permanent and effective filtration can be obtained regardless of which of the four main operations is performed. By not decompressing the eye, as is done when performing standard or classic trabeculectomy, there is a balance during the immediate postoperative period between the aqueous produced and the aqueous drained through the established micro communication preventing loss of the anterior chamber. Large cystic bleb complications such as those that take place with the use of standard doses of mytomycin do not occur later in the postoperative period.

In addition, these techniques can well be combined with phacoemulsification in patients with cataract and glaucoma that justify the combined operation. The surgical approach is through two places: corneal incision temporally for phaco and at 12 o’clock for the non-penetrating filtering operation. The glaucoma operation is performed first.

Main Differences Among Non-Penetrating Techniques

The main differences between them consist in the surgically altered anatomy, the different fluid dynamics and mechanism of outflow which takes place in each procedure and the destination of aqueous humor. Aqueous humor is filtered from the anterior chamber in different ways (Fig. 1, Chapter 20, Figs. 1, Chapter 21, 22, Figs. 1, 2, 3, Chapter 23 – **Editor**).

In **deep sclerectomy with intrascleral implant** the surgeon opens Schlemm's canal by dissecting a deep scleral flap, removing its roof or external wall with tiny forceps, peels out the endothelial layer of Schlemm's canal and moves further forward and dissects the thin remaining sclera, performing a significant thinning of the anterior trabeculum next to Descemets and exposing Descemet's membrane (Fig. 1-7, Chapter 22). Ultimately, only the trabeculo-descemetic membrane remains intact and only a very thin layer of the posterior part of the cornea divides the sclerectomy from the anterior chamber. The mechanism of aqueous outflow bypasses the juxta-canalicular meshwork (inner wall of Schlemm's canal) which is the site of highest resistance to aqueous outflow. Aqueous flows from the remaining trabecular meshwork - Descemet's membrane through the sclera into the subconjunctival space. In addition, an intrascleral collagen implant is introduced as an important part of the operation.

In comparing deep sclerectomy with the other procedures, Schlemm's canal is not cannulated as Stegmann does in viscocanalostomy. Anatomically, Arenas' ab-externo technique thins the tissue in the floor of SC somewhat posterior to the area of dissection in deep sclerectomy. Deep sclerectomy has a slow and difficult learning curve.

No Bleb Formation in Viscocanalostomy

Viscocanalostomy has no dependence on a filtering bleb. Watertight closure of the superficial scleral flap avoids the formation of a bleb since fluid is directed back to Schlemm's canal rather than accumulating in the subconjunctival space. Fluid then leaves Schlemm's canal via the intrascleral channels into the episcleral and conjunctival veins.

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Chapter 21
THE ARENAS AB EXTERNO TRABECULECTOMY TECHNIQUE

Eduardo Arenas A., M.D., F.A.C.S.

The Ab-Externo technique is based on a physiological concept: it removes the diseased endothelial layer of Schlemm's canal (SC in Fig. 1-B, Chapter 20) (which is the site of highest resistance to outflow present in open angle glaucoma) resulting in normal flow of aqueous humor outside the eye. We employ a micro diamond drill in order to unroof SC and avoid the risk of accidental perforation of the anterior chamber which is one of the most frequent complications of non-penetrating filtering operations, particularly during the learning curve (Fig. 1). Schlemm's canal (SC) is first unroofed by dissection of a deep scleral flap or with the microdrill (Fig. 1). With the drill the surgeon achieves a micro communication of the floor (inner wall) of Schlemm's canal to the anterior chamber (Fig. 1). The aqueous humor in Schlemm's canal begins to pour out. Then the surgeon drills out the microscopic layer of diseased endothelium (Fig. 1-E) that makes up the floor of Schlemm's canal, which constitutes the site of greatest resistance to outflow. What remain are several layers of very thin, trabecular fibers between the opened Schlemm's canal and the anterior chamber. The presence of these layers of trabecular meshwork at this site protect the integrity of the anterior chamber (no loss in depth) and prevent herniation of the iris. The trabecular meshwork remains as the only structure separating the anterior chamber from the conjunctiva after the Ab Externo procedure (Figs. 1 in Chapters 20 and 21). The aqueous filters through the remaining trabecular meshwork toward a subconjunctival bleb. (**Editor´s Note**: for step by step technique, see Figs. 2, 3, 4, 5, 6, 7, 8.)

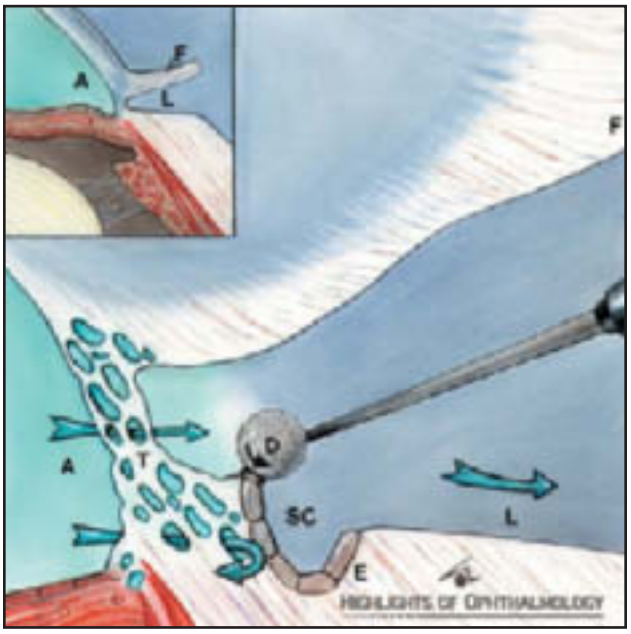


Figure 1: Arenas' Ab-Externo Technique

Schlemm's canal is first unroofed by dissection or with a micro diamond drill. The surgeon then uses the diamond drill (D) to remove the diseased endothelium (E) of the floor of Schlemm's canal (SC). What remains are several layers of very thin trabecular fibers (T) between the opened Schlemm's canal and the anterior chamber (A). These layers of trabecular meshwork protect the anterior chamber and prevent herniation of the iris. After the ab-externo procedure the trabecular meshwork is the only structure separating the anterior chamber (A) from the conjunctiva. This facilitates improved filtration through the trabecular meshwork into the subconjunctival tissues and leading to the formation of a filtering subconjunctival bleb. (L) indicates the space created by lifting and eventual removal of the scleral flap (F).

(This figure is a conceptual and accurate representation by HIGHLIGHTS.)

Main Advantages

The significant advantages of this procedure are the following:

1.) The ab-externo trabeculectomy is a non-invasive fistulizing procedure which allows spontaneous, continuous filtration of aqueous after removal of the external walls of Schlemm's canal (Figs. 2, 3, 4, 5). The internal wall of the canal is slightly severed with a diamond drill especially designed by Arenas for this operation (Fig. 7).

2.) Because it is an extraocular procedure, retrobulbar or peribulbar block is not necessary. Local anesthesia consists of 1 cc of subconjunctival infiltration with 1% lidocaine hydrochloride followed by digital massage to diffuse the anesthesia.

No flat chambers occur postoperatively because the anterior chamber is not entered for the fistulizing procedure. This is a microscopic filtering operation.

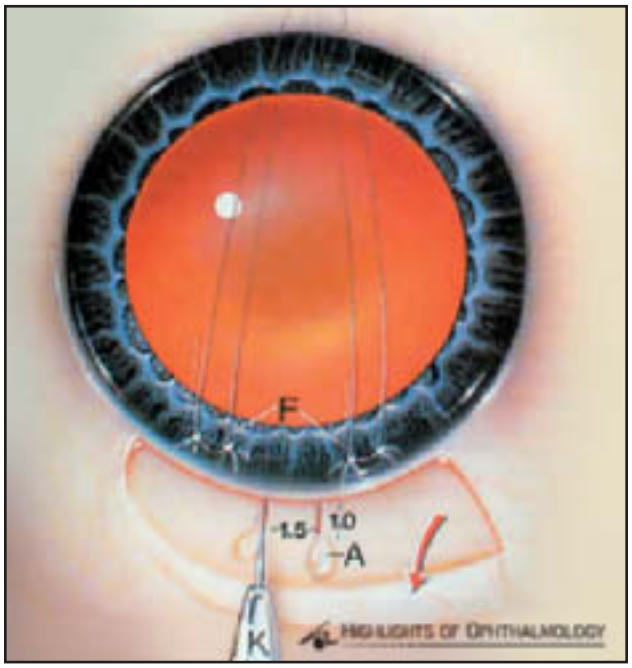


Figure 2: Ab-externo Trabeculectomy - Stage 1 - Initial Steps and Ab-externo Incision

The procedure begins with two 7-0 silk fixation sutures placed deeply in the cornea (F). A fornix based "L" shaped conjunctival flap is reflected (arrow) and limbal area cauterized with diathermy. Two parallel incisions are made 1.5 mm apart, starting at the limbus and extending posteriorly for 1 mm in an ab-externo fashion until a small leakage of aqueous (A) is obtained. This leakage shows that the external wall of Schlemm's canal has been reached. The knife (K) is shown making the left incision as fluid presents itself.

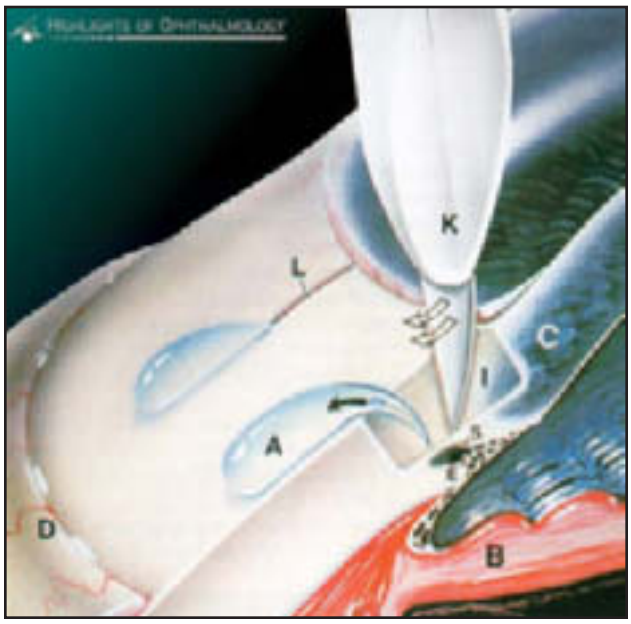


Figure 3: Ab-externo Trabeculectomy - Stage 1 - Initial Steps and Ab-externo Incision - Cross Section

The above oblique cross section view shows the 1 mm ab-externo incision (I) being made with knife (K). The knife makes passes of ever-increasing depth (white arrows) until a small leakage of aqueous (A - black arrow) is obtained. Notice that the knife has nearly reached a depth of Schlemm's canal (S). The completed left ab-externo incision (L) also presents aqueous. Other anatomy: Iris (B), cornea (C), reflected conjunctiva (D), scleral spur (E).

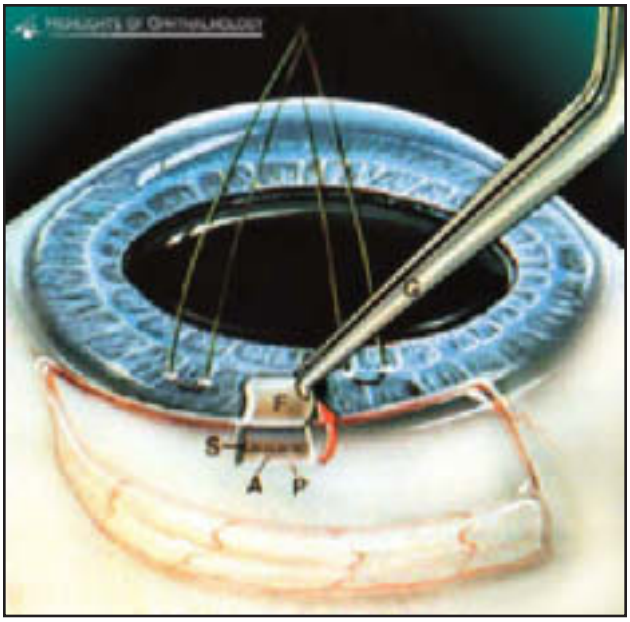


Figure 4: Ab-externo Trabeculectomy - Stage 2 - Creation of Microflap

At the moment when aqueous is obtained, the two parallel incisions are joined with an incision (P) at their posterior aspects. A small rectangular scleral flap (F) is formed and reflected (arrow) with a forceps (G). Usually a flow of aqueous (A) is observed at the base of the rectangular scleral bed. The origin of this aqueous is Schlemm's canal (S - dot shaded area) which can be observed on the scleral bed.



Figure 5: Ab-externo Trabeculectomy - Stage 2 - Creation of Microflap

This oblique cross section view shows the scleral flap (F) being reflected (arrow) with forceps (G), revealing Schlemm's canal (S) on the resulting scleral bed. Note the aqueous (A) at the bottom of the rectangular scleral bed.

3.) Mitomycin can be used in all cases because the drug's concentration is a good deal less (0.08 mg/cc instead of the usual 0.2 mg to 0.4 mg/cc). Arenas has found this dosage to be sufficient and effective. Because of the low concentration it can be applied to the bed of the scleral flap but with a sponge large enough that will reach and exert its effect on the overlying conjunctiva without touching the edges of the conjuntival flap. Otherwise, healing of the flap would be affected. (Fig. 6).

4.) The microscopic filtration is obtained by means of a highly sophisticated diamond drill which spins at 8000 revolutions per minute in the bed of the scleral flap until reaching and slightly severing the internal wall of Schlemm's canal (Fig. 7).

5.) This procedure can be easily adapted to using it as a combined operation with extracapsular extraction or with phacoemulsification.

6.) At the end of the operation, the surgeon should check the amount of aqueous exiting the eye. It should be microscopic but continuous. If insufficient, additional but slight drilling of the internal wall of Schlemm's canal can be made at that time before closure of the conjunctiva .

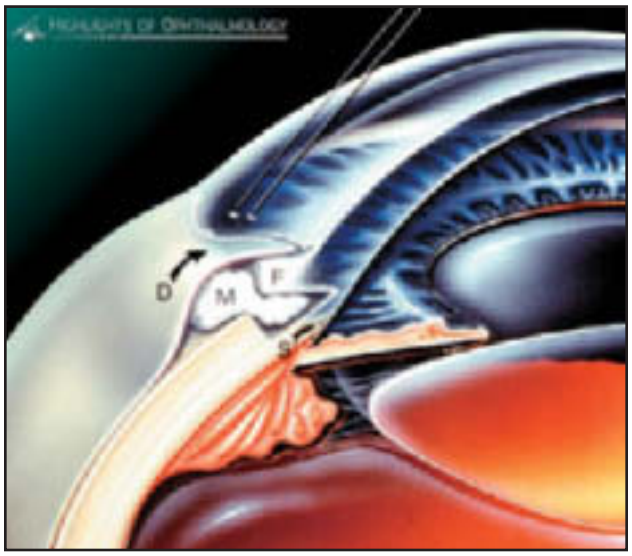


Figure 6: Ab-externo Trabeculectomy - Stage 3 - Application of Mitomycin

This oblique cross section shows the Weck sponge soaked with a 0.08 concentration of Mitomycin (M) placed over Schlemm's canal (S) and under the micro-scleral flap (F). The sponge must also reach the overlying conjunctiva and exert the effect of mitomycin on the conjunctiva and the bed of the scleral flap. The conjunctiva (D) covers (arrows) this area. The mitomycin sponge is left in place for three minutes.

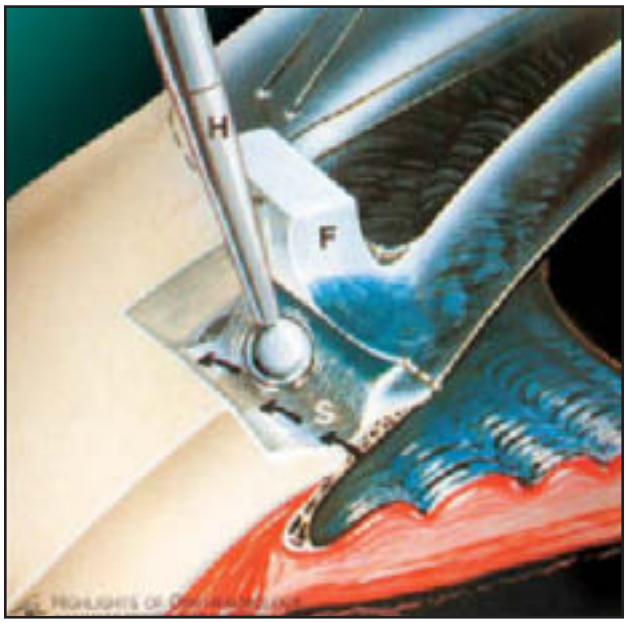


Figure 7: Ab-externo Trabeculectomy - Stage 4 - Drilling of Schlemm's Canal

The conjunctiva (D) and microflap (F) are reflected and Mitomycin sponge removed. Arenas diamond drill (H) spinning at 8000 revolutions per minute, is used to slowly deepen the area over Schlemm's canal (S) until the internal wall of the canal is severed. This will produce a more intense and permanent outflow of aqueous (arrows). This microscopic filtering procedure has completely preserved the anterior chamber.

Arenas advocates that with this technique continuous leaking of aqueous is produced that avoids the proliferation of fibrous tissue and promptly guarantees the formation of a bleb that will result in lowering of intraocular pressure.

Immediate and Short Term Evolution - Post-Op Management

Close monitoring of the intraocular pressure is important. Within the first 24 hours, the intraocular pressure is around 5 mm Hg. It slowly reaches 10 to 15 mm Hg by the end of the third week without any anti-glaucoma medication.

If the intraocular pressure reaches levels higher than 10 mm Hg by the first week post-op, Arenas performs a YAG laser trabeculolysis through a Goldmann gonioscopic lens to improve the passage way for aqueous flow under the microflap (Fig. 8). Usually two shots with an intensity of 6 to 7 millijoules focused at the filtering zone in the angle are sufficient to lower again the pressure at desirable levels.

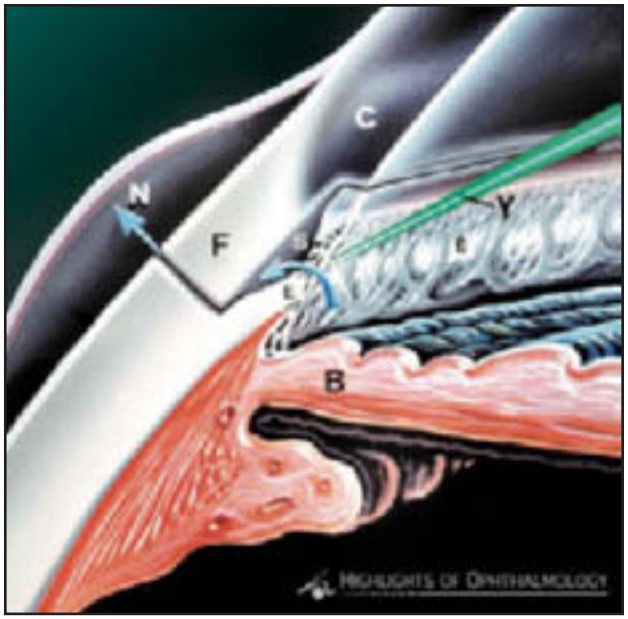


Figure 8: YAG Laser Trabeculolysis Postoperatively

If the intraocular pressure tends to be higher than 10 in the first postoperative days, a YAG trabeculolysis is performed. This gonioscopic cross section shows the YAG laser beam (Y) effecting a burn over the area of opened Schlemm's canal (S), under the microflap (F) of the filtering zone. This burn will create an improved passageway for aqueous flow (arrows) under the microflap and into the filtering bleb (N). Other anatomy: Scleral spur (E) seen gonioscopically and in cross section, cornea (C), and iris (B).

Chapter 22
DEEP SCLERECTOMY WITH INTRASCLERAL IMPLANT

André Mermoud, M.D.

General Considerations

When performing glaucoma surgery, the surgeon has two aims: one to lower the intraocular pressure to the target pressure or less and two, to avoid per and postoperative complications which may influence the surgical outcome or worsen the patient's vision.

Since the start of glaucoma surgery there has been a continuous trend to improve the success rate and to lower the complications of filtering surgery.

The Full Thickness Operations

The earliest surgical techniques were full thickness procedures with perforation of the sclera. This was done first by MacKenzie in 1830, and then was improved subsequently by De Wecker in 1869, La Grange, and others. In 1909 Elliot described the use of limbal trephination. This became the standard filtering operation until the 1940s. The main disadvantage of full thickness procedures was the overfiltration in the early postoperative period leading to ocular hypotony, shallow or flat anterior chamber associated with choroidal detachment. In the later follow up, the patients often developed thin filtering blebs predisposing the patient to endophthalmitis.

Trabeculectomy with Scleral Flap

Sugar in 1961, Cairns in 1968 and others later reported good results performing trabeculectomy under a superficial scleral flap. This flap created a resistance to aqueous outflow and lowered the incidence of postoperative ocular hypotony. Nevertheless, when the superficial scleral flap was sutured too tight, the postoperative IOP was too high, and when the sutures were not tight enough, the patient experienced ocular hypotony with the classical related complications such as shallow or flat anterior chamber, choroidal detachment, intraocular inflammation, and cataract formation. Several techniques have been proposed in the last few years to improve the reproducibility of trabeculectomy like releasable scleral sutures and postoperative suture lysis with the Argon laser. The so called modern trabeculectomies were definitively safer than the early trabeculectomies, but the follow up still required several examinations and additional procedures such as massage and Argon laser suture lysis.

The Onset of Non-Penetrating Filtering Operations

To improve the reproducibility and the safety of filtering procedures, several techniques of non penetrating filtering surgery have been described in the last years[1-11]. (**Editor's Note:** The pioneer of those techniques is Eduardo Arenas, M.D., who first described his ab-externo trabeculectomy in 1991 and 1993 and traveled world wide to teach its principles and techniques. See Ref. No. 6 of Bibliography). The principal concept of the non perforation is to create a filtration through a natural membrane which acts as a site of outflow resistance, allowing a progressive IOP drop and avoiding the postoperative ocular hypotony. The membrane is formed by the

trabeculum and the limbal descemetic membrane: the trabeculo-descemet's membrane (TDM) [1]. To create the membrane the surgeon has to perform a deep sclerokeratectomy providing a postoperative scleral space. This space may act as an aqueous reservoir and as a filtration site which may avoid the need for a subconjunctival filtration bleb. Thus the risk of late hypotony and / or bleb related endophthalmitis may be reduced.

In patients suffering from primary and secondary open angle glaucoma, the main site of aqueous outflow resistance is thought to be at the level of the juxtacanalicular trabecular meshwork and the inner wall of Schlemm's canal. By removing the internal wall of Schlemm's canal and the juxtacanalicular meshwork, the main outflow resistance in glaucomatous patients should thus be relieved.

The technique has been called ab externo trabeculectomy.[5-8] (**Editor's Note**: We refer you to Fig. 1 of Chapter 20 to clearly observe the difference between the **normal** anatomy and fluid dynamics as compared with the anatomy and fluid dynamica of a glaucoma patient. In Fig. 1 of Chapter 21 you can see the surgical principles of Arenas' ab-externo trabeculectomy and how it works. In Fig. 1 of this Chapter, you can see the principles of a deep sclerectomy and how it functions.)

In primary and secondary closed angle glaucomas and probably in congenital glaucoma, the outflow resistance is located before the trabeculum meshwork. Thus non perforating filtering surgery is not indicated for the treatment of these glaucomas.

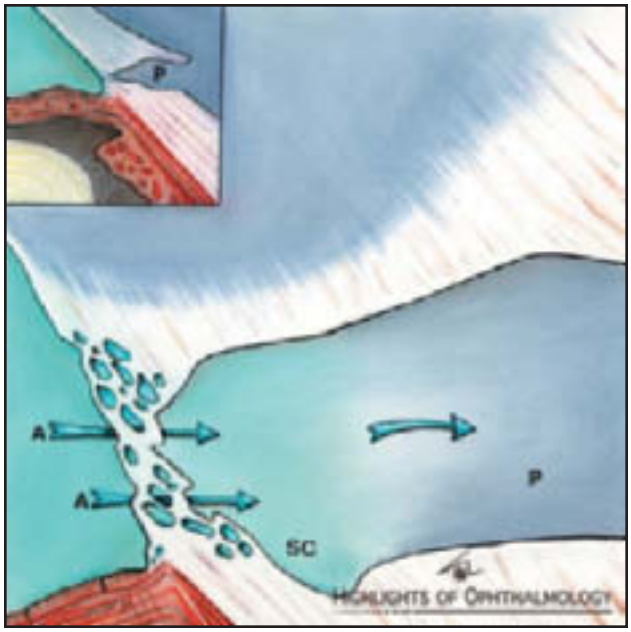


Figure 1: Deep Sclerectomy

Schlemm's canal (SC) is unroofed by surgical dissection. The corneal portion of the trabeculum (T) is surgically thinned. Only a very thin layer of the posterior part of the cornea divides the sclerectomy from the anterior chamber. Arrow (A) indicates improved filtration in the thinned region by bypassing the juxta-canalicular meshwork (inner wall of Schlemm's canal) leading to the subconjunctival space. (P) indicates the passage created by lifting the scleral flap. ***(This figure is a conceptual and accurate representation by HIGHLIGHTS.)***

Surgical Technique

Anesthesia

All types of anesthesia have been used successfully for non penetrating filtering surgery. We recommend injecting the smallest amount of peri-or retrobulbar anesthesia in order to adequately rotate the globe for maximum view during the deep sclerectomy dissection. Three to four mls of a solution of bupivacaine 0.75%, xylocaine 4% and hyaluronidase 50U are usually sufficient for a successful local anesthesia. Topical and subconjunctival anesthesia are also possible and have been performed successfully in selected cases.

Obtaining Adequate Exposure

A superior rectus muscle traction suture is placed and the eye ball is rotated to expose the site of the deep sclerectomy (usually the superior quadrant). To avoid superior rectus muscle bleeding, a superior intracorneal suture may be placed.

Conjunctival Flap

The conjunctiva is opened either at the limbus or in the fornix. The limbal incision offers a better scleral exposure but needs a more careful closure, especially when antimetabolites have been used. (**Editor's Note:** With limbus based flaps the major problem may be buttonholing of the conjunctiva at the limbus).

Preparation of the Scleral Field

The sclera is exposed and hemostasis is obtained using a wetfield electrocoagulation cautery. To facilitate the dissection to obtain a clean bare sclera all Tenon's capsule residue is removed with a hockey stick knife. Sites with large aqueous drainage veins must be avoided to preserve physiological drainage.

Superficial Scleral Flap

A superficial scleral flap measuring 5 by 5 mm is dissected including 1/3 of the scleral thickness (about 300 microns).

In order to be able to dissect the corneal stroma down to Descemet's membrane later, the scleral flap is dissected 1 to 1.5 mm into clear cornea (Fig. 2 A-B). To facilitate the horizontal scleral dissection, a ruby blade or a metallic crescent blade may be used.

Antimetabolities

In patients with high risks of sclero-conjunctival scar formation, (eg: young patients, blacks, secondary glaucoma, and those having previous surgery), a sponge soaked in Mitomycin-C 0.02% is placed for 45 seconds to 1 minute in the scleral bed and between the sclera and Tenon's capsule. (**Editor's Note**: According to Dr. Mermoud's description, two different sites are used: 1) Over full thickness sclera, as described in Chapter 19; 2) Under the superficial scleral flap over the sclera - (Fig. 2). After the removal of the sponge, the site is washed with balanced salt solution (20-30 ml).

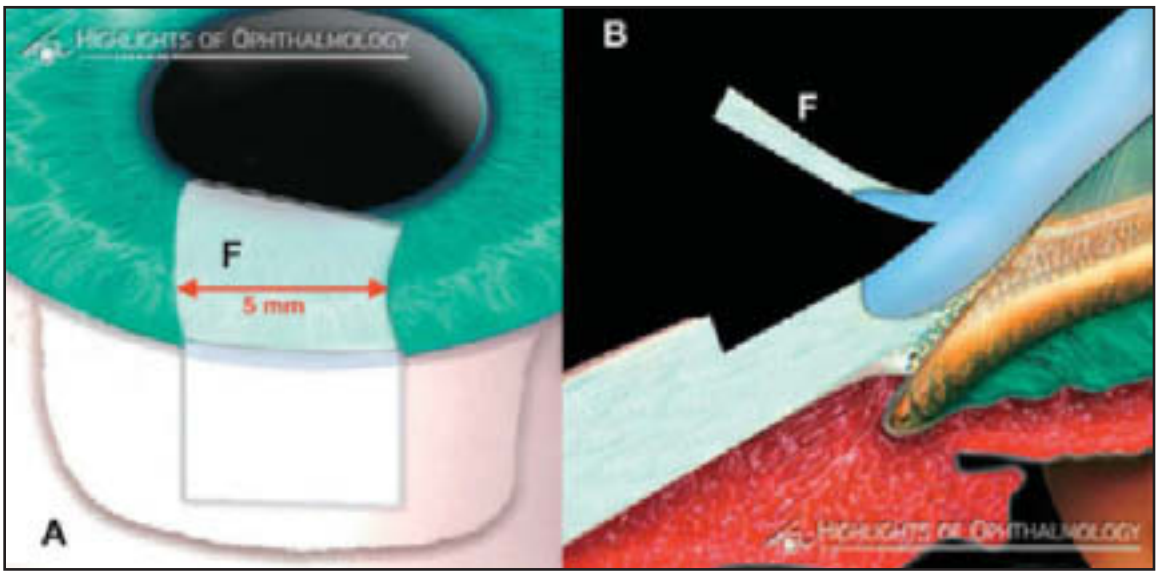


Figure 2 (A-B): The Surgical Scleral Flap - Surgeon's and Cross Section Views.
A superficial 5 x 5 mm scleral flap (F) is created, 1/3 of scleral thickness in depth and is extended 1 to 1.5 mm into clear cornea.

Deep Sclero-keratectomy or Deep Scleral Flap (Deep Sclerectomy)

Deep sclero-keratectomy is done by performing a second deep scleral flap. The two lateral and the posterior deep scleral incisions are made using a 15 degree diamond blade. The deep flap is smaller than the superficial one leaving a step of the sclera on the three sides (Fig. 3). This will allow a tighter closure of the superficial flap in case of an intraoperative perforation of the Trabeculo Descemet's membrane. The sclera is dissected down almost 95% of its thickness (about 600 microns). If complete perforation of the sclera occurs in some parts of the incision, the surgeon can see the ciliary body anteriorly and the choroid posteriorly in the remaining ultrathin scleral bed. In our experience, this has not been followed by any complications. The deep scleral flap is then dissected horizontally using a crescent ruby blade (2 mm angled bevel up). The remaining scleral layer should be as thin as possible (50 to 100 microns) (Fig. 3 A-B). The dissection of the deep sclerectomy is preferably started first in the posterior part of the deep scleral flap.

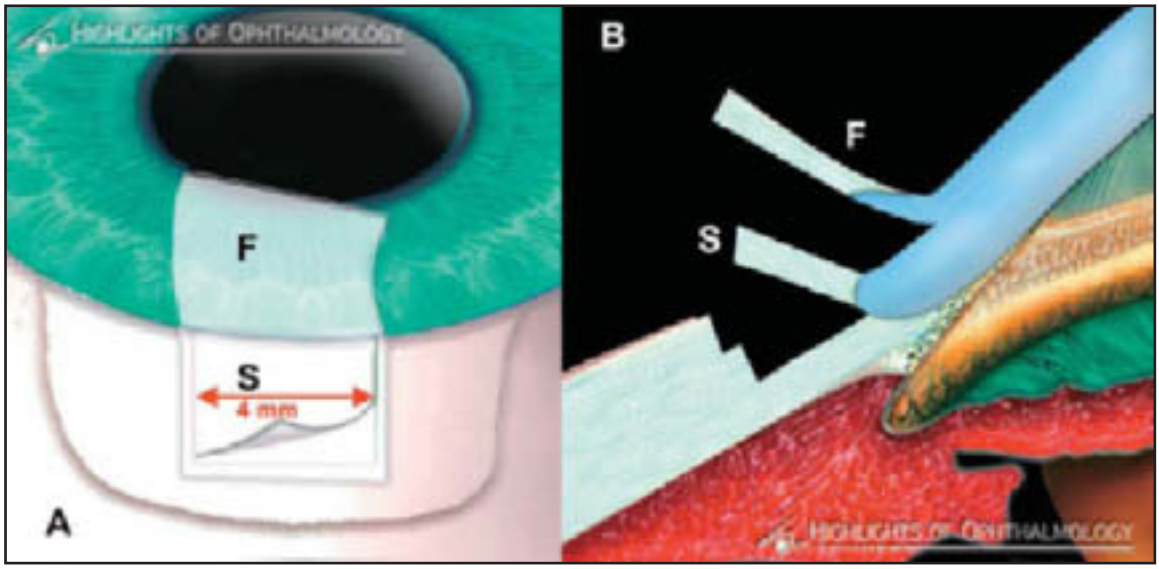


Figure 3 (A-B): Deep Sclerectomy (Deep ScleroKeratectomy) - Surgeon and Cross Section Views.
The second deep sclerectomy measures 4 x 4 mm (S) and the sclera is dissected down to 95% of its thickness, leaving about 5% of the sclera over the choroid and ciliary body. Anterior scleral flap (F).

This helps to avoid anterior chamber perforation. Posteriorly, the scleral fibres are layed at random directions. More anteriorly, they become more regularly oriented eventually forming a ligament parallel to the limbus corresponding to the Scleral Spur. Schlemm's canal is located anterior to the Scleral Spur. The latter is an excellent landmark for the identification of Schlemm's canal (Fig. 4 A-B). Schlemm's canal is opened and the sclero-corneal tissue representing the Scleral Spur (Fig. 4 A-B) are behind the anterior trabeculum and Descemet's membrane. This step of the surgery is difficult because there is a high risk of perforation of the anterior chamber. The dissection between Descemet's membrane and the corneal stroma is very carefully done with a sponge or a spatula. In order to complete the proper exposure of Descemet's membrane, two radial corneal cuts have to be done without touching the Anterior Trabeculum nor Descemet. This is performed with the 15 degrees diamond knife. When the anterior dissection is completed, the deep scleral flap is cut anteriorly using the diamond knife and a

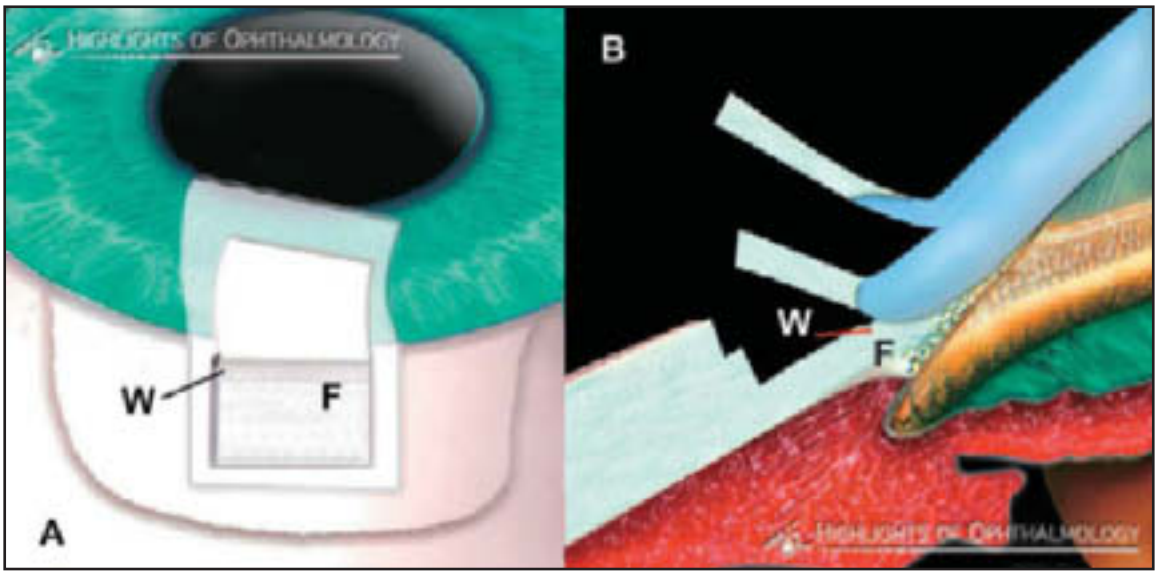


Figure 4 (A-B): Opening of Schlemm's Canal.
Schlemm's canal is opened (W). Posterior to Schlemm's canal, the horizontal scleral fibers represent the Scleral Spur (F).

Galand scissors (length 5.5 mm, curved and blunt blade) (Fig. 4 A-B and Fig. 5 A-B). At that stage of the procedure, there should be a nice percolation of aqueous through the remaining trabeculo-Descemet's membrane.

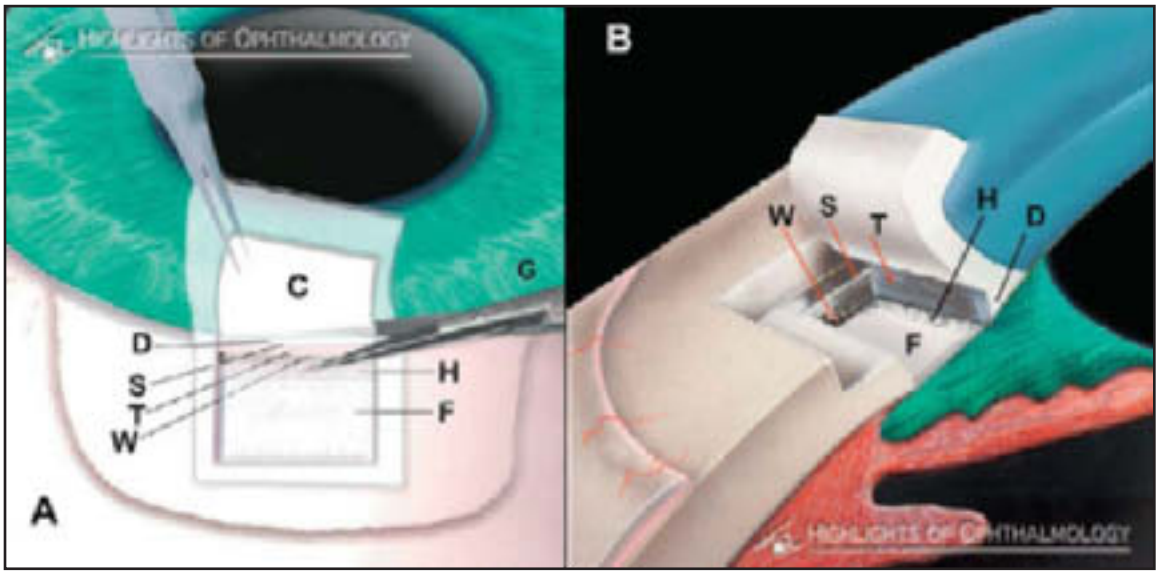


Figure 5 (A-B): Exposing Anterior Trabeculum, Descemet's and Removing Deep Sclero Corneal Tissue - Surgeon and Cross Section Views.

Two radial cuts have been done with a diamond blade to expose the anterior trabeculum (T) and Descemet's membrane (D). The deep sclero-corneal flap (C) is removed with Galand scissors (G). The peeling of the inner wall of Schlemm's canal (W) and juxtacanalicular trabeculum is also called <ab externo Trabeculectomy >. Schwalbe's line (S). Scleral spur (H). Scleral fibers (F).

Inner Wall Schlemmectomy and External Trabeculectomy

Since in primary and probably in some secondary open-angle glaucomas, the main site of aqueous outflow resistance, is thought to be at the juxtacanicular trabeculum and Schlemm's endothelium, this structure should be removed using a small blunt forceps (deep sclerectomy forceps 13,0 mm jaws, Huco vision SA, St-Blaise, Switzerland). (**Editor's Note**: To precisely identify the site of outflow resistance, see Figs. 1 in Chapter 20, 21, and in this Chapter 22). This additional procedure has been called ab externo trabeculectomy [6, 7]. (See Chapter 21). To peel the thin Schlemm's endothelium and juxtacanalicular trabeculum portion, it is crucial to dry the exposed inner wall of Schlemm's canal. When dried, the inner wall of Schlemm's canal can be grabbed with the forceps and peeled easily by pulling on it. This maneuver is followed by more important percolation of aqueous through the posterior trabeculum

Intrascleral Implant

To avoid a secondary collapse of the superficial flap over the Trabeculo-Descemet's membrane and the remaining very thin scleral bed, a collagen implant is placed in the scleral bed and secured with a single 10/0 nylon suture (Fig. 6 A-B). The remaining superficial scleral flap is closed and secured to Tenon's with two loose nylon sutures. The conjunctiva and Tenon's capsule are closed with one running 8/0 Vicryl suture.

The collagen implant is processed from porcin scleral collagen. It increases in volume after contact with aqueous and is slowly reabsorbed within 6 to 9 months leaving a scleral space for aqueous filtration [12-15].

Other implants may be used to fill the sclerocorneal space left after the dissection and removal of the deep sclerocorneal flap such as high viscosity hyaluronic acid (also called viscocanalostomy by Stegmann, ref 9), reticulated hyaluronic acid (Sourdille, unpublished data), or Hema implant (Dahan, unpublished data). Other types of materials will be available in the future.

Postoperative Medications

Patients are treated topically with a corticosteroid and an antibiotic for 2-3 weeks followed by nonsteroidal anti-inflammatory drugs for up to three months postoperatively. No cycloplegic nor miotic agent are prescribed. Usual eye care and protection are recommended to the patient.

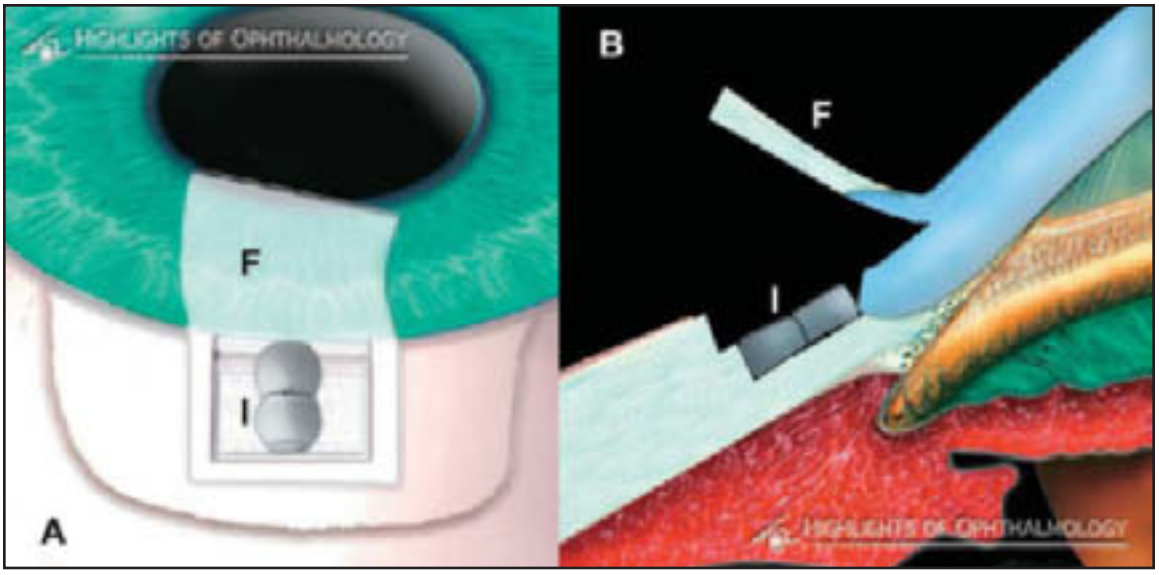


Figure 6 (A-B): Positioning of Scleral Implant.

To avoid collapse of the superficial scleral flap (F), a collagen implant (I) is positioned in the remaining very thin scleral bed and secured with a 10/0 nylon suture. The implant as shown in the cross section is repositioned and sutured with two loose 10/0 nylon sutures.

Intraoperative Complication

When a large perforation of the thin trabeculo-Descemet's membrane occurs during the corneal stroma dissection (See Figs. 3 and 4 for anatomical structures. **Editor**), the surgery is converted into a standard trabeculectomy, with a rectangular resection of the trabeculum, followed by a basal iridectomy. To avoid an anterior chamber collapse, high viscosity viscoelastic is injected into the superior part of the anterior chamber and into the scleral dissection. The superficial scleral flap is then closed carefully with 5 to 8 nylon 10/0 sutures.

Postoperative Complications

Insufficient Filtration

Goniopuncture with the Nd:YAG laser may be performed when the filtration through the Trabeculo-Descemet's membrane is suspected to be insufficient, because of elevated IOP and relatively flat bleb [16]. For the laser treatment, we use a Lasag-15 gonioscopy contact lens (CGA1). Goniopuncture is performed using the free-running Q-switch mode with energy ranging from 4 to 5 mj. The goal of the laser treatment is to create a small hole in the trabeculo-descemet's membrane, which is technically similar to a posterior capsulotomy after cataract surgery. The easiest way to perforate the trabeculodescemet's membrane is to aim at the Descemet's window seen on gonioscopy (Fig. 7). In order to have a thin Descemet window it is crucial to have previously dissected the deep sclero-corneal flap 1 to 1.5 mm anterior to Schwalbe's line and deep enough leaving no corneal stroma over Descemet's membrane. Laser Goniopuncture allows direct passage of aqueous from the anterior chamber to the intrascleral space and the filtration bleb and transforms the non-perforating filtering surgery into a perforating filtering surgery. After laser treatment, patients are treated with topical prednisolone acetate (Predforte ®) 3 times a day.

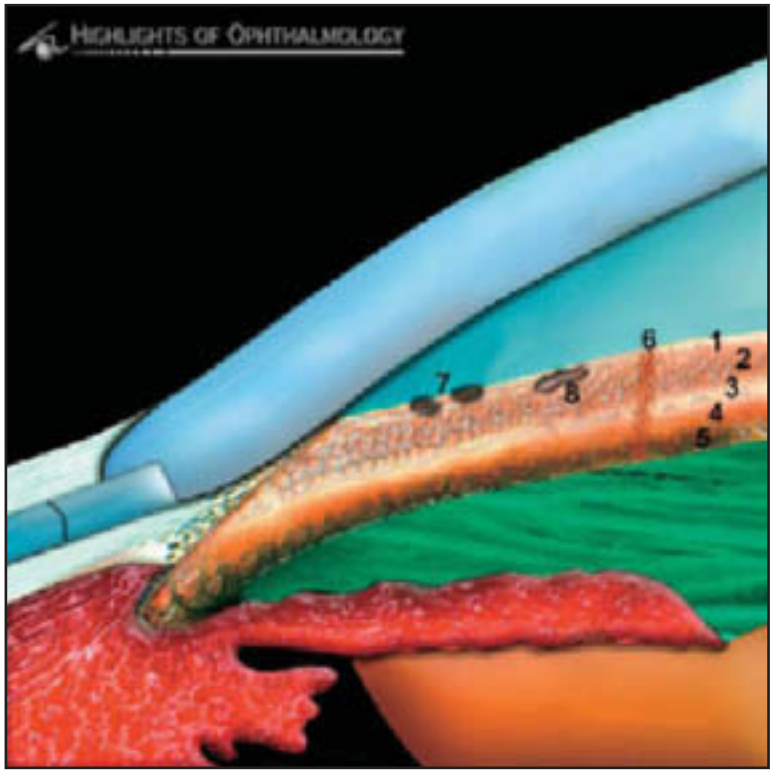
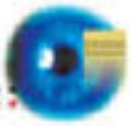


Figure 7: Nd:Yag Goniopuncture for Insufficient Filtration.

The easiest site to perforate the trabeculo-descemet's membrane (6) is through Descemet's Window (7) or the junction between Descemet's membrane and the anterior trabeculum (Schwalbe's line) (1). Rupture of Schwalbe's line after goniopuncture (8).



Combined Surgery for Cataract and Glaucoma

For patients presenting with cataract and glaucoma, it is recommended to perform a combined phacoemulsification and non penetrating filtering surgery. Ideally, the two procedures should be performed at different sites: the phacoemulsification is done through a clear temporal corneal incision and the non penetrating filtering operation located superiorly at 12 o'clock. The surgical technique for the non-penetrating filtering operation is, in our hand, a deep sclerectomy with intrascleral collagen implant. The **phacoemulsification** and **IOL implantation should be done first**, since high intraocular pressure during hydrodyssection and phacoemulsification may rupture the fragile trabeculodescemet's membrane. [17,18]

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Chapter 23
VISCOCANALOSTOMY

Robert Stegmann, M.D.

This technique involves the dissection of superficial and deep scleral flaps, extended into clear cornea for 0.5 mm (Fig. 1). The first or superficial scleral flap is dissected approximately 1/3 thickness of the sclera. The second deeper flap constitutes approximately two thirds of the scleral thickness to leave a thin translucent layer of sclera overlying the choroid (Fig. 1). As the second flap is dissected forward in the correct plane, Schlemm's canal is visualized approximately 1.0 mm posterior to the limbus (Fig. 1).

Exposure of Schlemm's canal shows the important landmark of smooth gray-white tissue, which constitutes the roof of the canal. As **Schlemm's canal is unroofed**, a finely polished cannula with an outer diameter of 150 µm is introduced

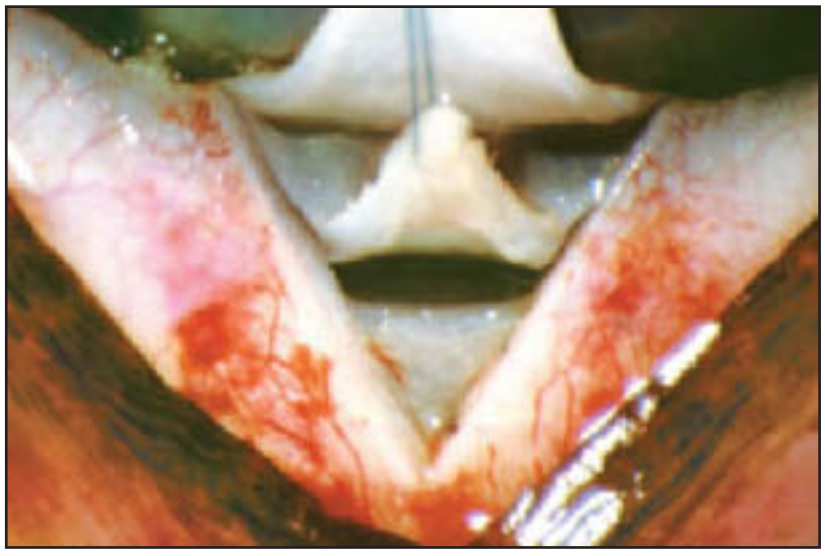


Figure 1: Stegmann's Viscocanalostomy - Creation of the Sub-scleral Lake

In this technique a sub-scleral lake is created by removal of the inner scleral flap. This inner flap lies beneath the larger, more external flap. Removal of this flap exposes and unroofs Schlemm's canal and creates a lake for collection of aqueous humor.

into the ostia or surgical openings of Schlemm's canal, in a right and left direction, to inject high-viscosity viscoelastic for 4.0 to 6.0 mm on each side (Fig. 2 A-B). The viscoelastic injection increases the diameter of Schlemm's canal from its usual diameter of 25 to 30 µm to about 230 µm and increases the patency of the outflow channels.

Aqueous is removed from the anterior and posterior chambers by a paracentesis puncture made with a mini diamond blade. Descemet's membrane is separated 1 to 2 mm from the corneoscleral junction by applying gentle pressure on Schwalbe's line using a cellulose sponge (Fig. 3 A-B). This maneuve **creates an intact window in Descemet's**

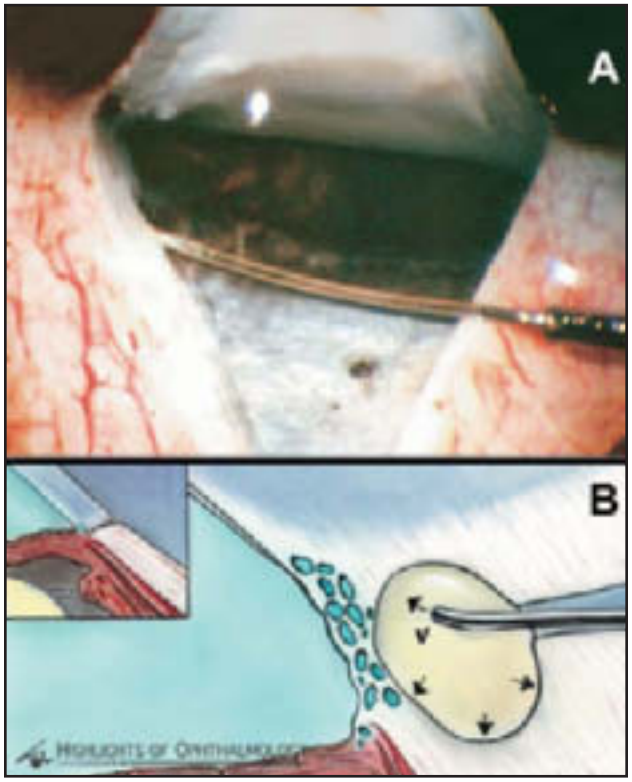


Figure 2 A-B (left): Stegmann's Viscocanalostomy - Enlargement of Schlemm's Canal

The next step of this procedure improves filtration by enlarging the diameter of Schlemm's canal with the injection of a high- viscosity viscoelastic (V) into the cut end of the canal. Figure 2A shows the lifted outer flap with Schlemm's canal exposed and the cannula being used for injection in Schlemm's canal, right and left. Figure 2B is a conceptual and accurate representation by HIGHLIGHTS of Schlemm's significant expansion (V- with arrows).

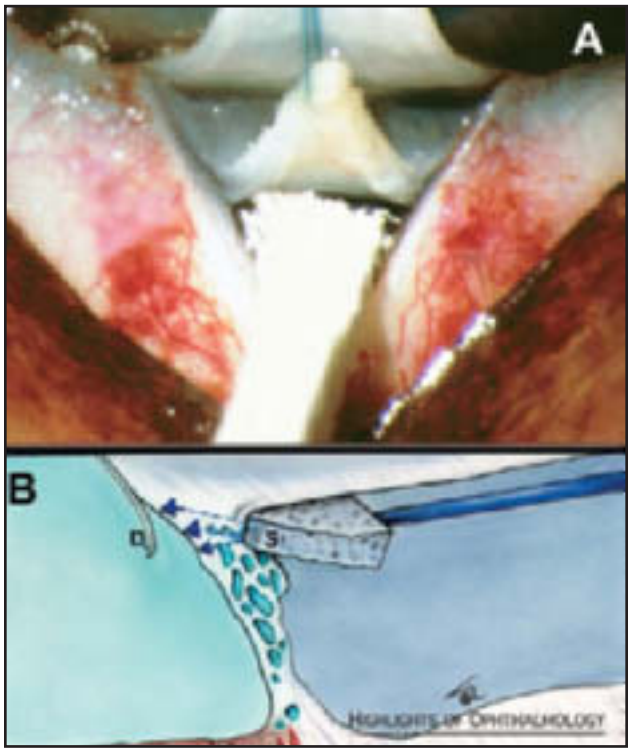


Figure 3 A-B (right): Stegmann's Viscocanalostomy - Separating Descemet's From Corneo-Scleral Junction

Gentle pressure is exerted with a cellulose sponge (S) on Schwalbe's line to separate Descemet's membrane (D) from the corneoscleral junction. This creates an intact window through which aqueous humor is diffused from the anterior chamber to the newly created subscleral lake.

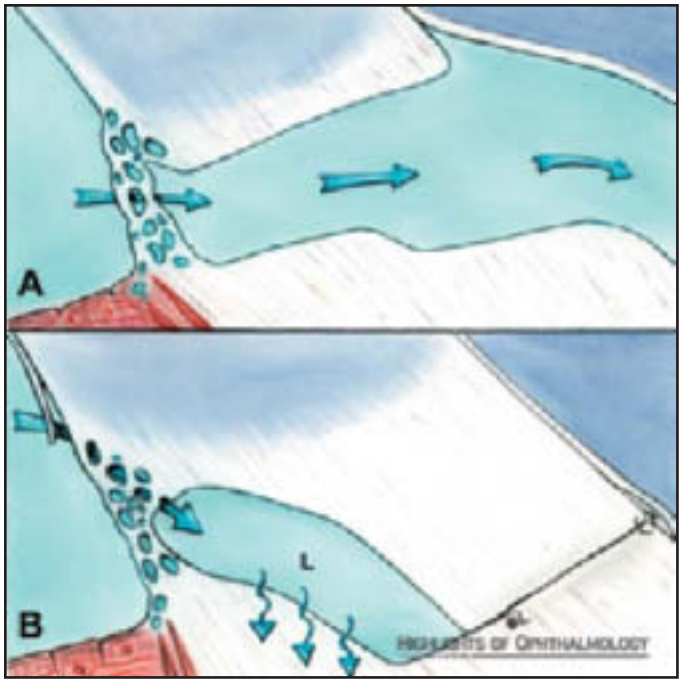


Figure 4: Comparison of Arenas' Ab-Externo Trabeculectomy and Stegmann's Viscocanalostomy

Both the ab-externo trabeculectomy and viscocanalostomy improve filtration of aqueous humor through Schlemm's canal. The ab-externo technique (A) improves filtration by removal of the diseased endothelial lining of Schlemm's canal. Aqueous flows through the trabecular meshwork (arrows) and into Schlemm's canal without being hindered by diseased endothelium. Aqueous then flows through a surgically enlarged passage in the sclera to form a filtering subconjunctival bleb.

Viscocanalostomy (B) improves filtration by enlargement of the diameter of Schlemm's canal and by the creation of a subscleral lake (L). Aqueous humor flows into this lake from the anterior chamber (straight arrows), through the trabecular meshwork and to the newly enlarged Schlemm's canal. A section of the sclera is removed to create a passage from Schlemm's canal to drain aqueous from the canal to capillaries and veins within the subconjunctival tissue and intrascleral channels (tortuous channels).

membrane through which aqueous humor is diffused from the anterior chamber into the subscleral lake. This procedure allows aqueous humor to reach Schlemm's canal bypassing the inner wall (floor) of Schlemm's canal (juxtacanalicular system) which is responsible for the highest resistance to outflow, as shown in Fig. 1-B of Chapter 20. The juxtacanalicular system is bypassed by exposing Descemet's membrane and not by physically removing it. Aqueous flows from the enlarged Schlemm's canal into the canalicular system to finally reach the venous circulation (Fig. 4-B).

The deeper scleral flap is then **excised** at its base using a Vannas scissors. The superficial flap is **sutured** using five 11-0 polyester fiber suture in a watertight manner.

A bleb is not formed since the sclera is sutured in a watertight manner to promote backflow of aqueous into Schlemm's canal thus avoiding subconjunctival flow.

Viscoelastic is subsequently injected into the subscleral lake. The conjunctival flap is sutured using 11-0 Mersilene sutures.

We consider the possibility that the injection of viscoelastic as here described may also contribute to expand the secondary channels that lead to drainage of aqueous humor into the outside circulation resulting in an increased flow. (**Editor's Note**: Figure 4 clarifies and enhances the understanding of Stegmann's Viscocanalostomy versus Arenas' Ab-Externo Trabeculectomy.)

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Chapter 24
NON-PENETRATING SURGERY FOR GLAUCOMA

Roberto Sampaolesi, M.D.
Juan Roberto Sampaolesi, M.D.

Editor's Note: Professor **Roberto Sampaolesi** is one of the world's most widely recognized glaucoma experts. His knowledge is profound, his experience is extensive (over 6,500 glaucoma patients). His research is sound and highly productive. He is admired as a skilled physician, distinguished teacher, and eminent investigator and productive author. **Sampaolesi** has written this chapter by special request from the Editor and, with the collaboration of his dedicated son, Juan Roberto Sampaolesi, has provided much insight into this rather "new" subject of non-penetrating filtering surgery for glaucoma

Background

Goldmann, by means of manometric experiments carried out between 1946 and 1949, was the first to find the resistance site (R). Upon measuring the pressure at the level of the aqueous veins and inside Schlemm's canal, he found identical values. He also measured it in the anterior chamber and in the Schlemm's canal, where there was a marked and significance difference. Based on this he inferred that the **site of the aqueous humor outflow resistance (R) was located between the anterior chamber and the Schlemm's canal, i.e. at the trabecular meshwork**. Perkins (1953) concluded similarly and Sears (1964), by using a more sophisticated method, reported that the resistance site is located at the level of the Schlemm's canal.

At present it has been widely accepted that 75 % of the outflow resistance is located at the inner wall of Schlemm's canal and the juxtacanalicular tissue, while the rest is located at the external wall, collectors, episcleral veins, etc.

Non-penetrating surgery is closely linked to Schlemm's canal surgery.

Our experience of 800 surgical procedures in early congenital glaucomas within two years of age throughout 40 years of practice (Sampaolesi 1994) has given us the expertise necessary for the identification of Schlemm's canal. Trabeculotomy, even after the publications of Burian in 1960, Burian & Allen in 1962 and Sugar in 1961, was a difficult technique to master until 1968, when Cairns introduced trabeculectomy as a surgical technique for open-angle glaucoma. Indeed, the novel introduction of a scleral flap with a hinge at the limbus (created by Cairns) made it possible for Harms, Paufique and Sourdille (Harms 1966, Harms & Dannheim 1970 and Paufique et al 1970) to develop a precise technique for trabeculotomy.

It was Krasnov, in 1962, who originally proposed the removal of the external wall of the Schlemm's canal and coined the word sinusotomy for this procedure, by which he removed the external wall of Schlemm's canal from 10 to 2 o'clock over 120∞; the inner wall of Schlemm's canal was untouched and then the conjunctiva was closed. However, this technique was not published until 1964. Alkseev (1978) proposed the removal of the endothelium of the inner wall of Schlemm's canal and of the juxtacanalicular tissue during sinusotomy, as this may increase the permeability of the inner wall of the sinus.

Zimmerman et al (1984) introduced non-penetrating trabeculectomy; Fyodorov et al (1984) proposed deep sclerectomy and later, and together with Kozlov and others (1989), non-penetrating deep sclerectomy; Kozlov et al (1990) improved the method with the addition of a cylindric collagen

implant and later developed laser goniopuncture, methods which were further developed by Kozlov & Kozlova (1996) and Kozlova et al (1996 and 2000). According to Kozlov's technique, in addition to the resection of the external wall of Schlemm's canal, the inner wall of Schlemm's canal with the endothelium, together with the juxtacanalicular tissue and external corneoscleral trabecular meshwork are removed. In 1991, Arenas Archila proposed trabeculotomy ab externo, which removed the same tissues, after removing the external wall of Schlemm's canal, but using a microtrephine working at a speed of 800 rpm. In 1999 Stegmann reported his results with visco-canalostomy in black African patients. Sourdille et al (1999) used a triangular reticulated hyaluronic acid implant with the same dimensions as those of the second triangular scleral flap, which we have successfully tested.

This technique, as currently known, is successfully used by Demailly (1996). Moreover, a very complete book has been edited recently by Andre Mermoud, who has an extensive experience on non-penetrating surgery.

Material

We have so far been using this surgical technique for 5 years.

Of the total 30 eyes of 40 patients ranging from 9 to 55 years of age studied, 18 had open-angle glaucoma, 3,pseudoexfoliation glaucoma, 2,pigmentary glaucoma; 4, late congenital glaucoma; 1, postraumatic glaucoma and 3, open-angle glaucoma associated with cataract (combined surgery).

Baseline and Follow-Up Examinations

All patients underwent non-penetrating deep sclerectomy according to Kozlov's technique, with the use of Minsky's transillumination technique, by which all the components of the chamber angle become evident, thus allowing proper placement of the incision.

The evolution was monitored pre- and post-operatively at 6-month-intervals by means of single-spot checks and daily pressure curves (Sampaolesi, 1961; Sampaolesi and Reca, 1964 and Sampaolesi, Calixto, Carvalho and Reca, 1968); the optic nerve condition was assessed by means of confocal tomography (Heidelberg Retina Tomograph: HRT) and compared to the normal and pathological tomographic values for each parameter according to our guidelines (Sampaolesi R and Sampaolesi JR, 1999), while the flow was measured with Doppler by using the HRF (Heidelberg Retina Flowmeter). Finally, the visual field was evaluated with computerized perimetry (Octopus 101, program G2 and PeriData software).

Surgical Technique

A rectangular one-third scleral thickness limbal-based scleral flap, the same as that created for a trabeculectomy, is dissected. One side of this rectangle, of 5 mm, is parallel to the limbus, while another one is perpendicular to it and 6 mm in length. Anteriorly, the scleral flap is dissected closer to the cornea than usual in trabeculectomy procedures. Corneal lamellae are dissected along 1.5 mm.

A second limbal-based triangular scleral flap is then created by penetrating 1,5 mm along the corneal tissue. A useful landmark for this dissection, which must be performed carefully, is the orientation of the scleral fibers, which though arranged in multiple directions at the scleral level, behind this flap, they become neatly parallel and circular at the level of the scleral spur, thus adopting a more whitish and nacreous appearance. Aqueous humor percolation at this stage, with the anterior chamber closed, when the dissection goes from the scleral spur towards the cornea, is indicative of placement of the incision at the proper plane. The triangular flap, containing the external wall of the Schlemm's canal, including its endothelium, is then resected. Anteriorly, the dissection should be made down to the deep corneal lamellae so that only the corneal endothelium, Descemet's membrane and a small layer of corneal lamellae are left. The dissection plane can generally be easily cre-

ated at this final stage by pulling the vertex of the triangular flap towards the cornea with a clamp.

Once the triangular flap has been removed, the surgeon resects a membrane formed by the inner wall of Schlemm's canal with its endothelium, the juxtacanalicular tissue and the external corneoscleral trabecular meshwork, while both internal corneoscleral trabecular meshwork and uveal trabecular meshwork remain intact, attached to the Descemet's membrane and the corneal endothelium. These tissues which remain intact constitute the so-called **trabeculo-descemet's membrane**, which is so resistant that it keeps the anterior chamber formed, avoids ocular hypertension and spares the complications of trabeculectomy.

The next step involves placement of the hydrophylic implant, either the cylindrical one (Staar) or the triangular one (Corneal), which is secured by placing a nylon 10/0 suture, followed by closure of the conjunctival flap with two stitches, and of the conjunctiva at the level of the corneoscleral limbus.

The description above depicts what happens when the procedure is performed by an experienced surgeon. Otherwise, it is very important for the inexperienced surgeon to correlate what he sees in the surgical field with its anatomical elements.

Anatomic and Histologic Considerations in the Surgical Technique

Figure **1** is a schematic representation of the chamber angle. The sclera ends anteriorly with three prongs: two long ones, one anterior, which forms the **sclerocorneal limbus** and one posterior one, which forms the **scleral septum**. Its anterior edge is **Schwalbe's line**. The third prong is shorter and constitutes the **scleral spur**. The two first ones form an **optic canal** which lodges the **cornea**, while between the second and the third one a **filtration canal** is formed to lodge the **Schlemm's canal** and the **trabecular meshwork**.

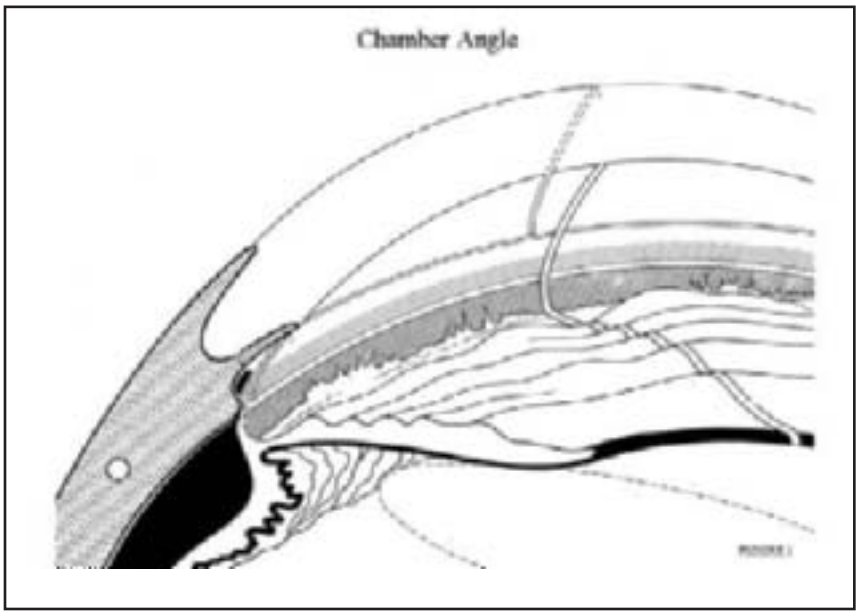


Figure 1: Schematic representation of the chamber angle. The sclera ends anteriorly with three prongs: two long ones, one anterior, which forms the **sclerocorneal limbus** and one posterior one, which forms the **scleral septum**. Its anterior edge is **Schwalbe's line**. The third prong is shorter and constitutes the **scleral spur**. The two first ones form an **optic canal** which lodges the **cornea**, while between the second and the third one a **filtration canal** is formed to lodge the **Schlemm's canal** and the **trabecular meshwork**.

If the dissection has been performed correctly, the image on figure 2, showing three clear areas is visualized. The limbar area, area 1, is dark. The last iris rolls can be seen by transparency through the endothelium and Descemet's membrane if, according to Minsky's maneuver, the area is transilluminated by means of the optical fiber of the microscope supported by the cornea, and separated from it by one of the white triangles used for drying, but embedded in physiological solution to prevent the cornea from overheating.

Area 2 can be identified by its blue color, it is located more backwards and called blue area. The anterior limit of this area corresponds with Schwalbe's line, which anatomically constitutes the anterior edge of the scleral septum, while the posterior limit of this blue area corresponds with the scleral spur, with the Schlemm's canal located anteriorly. The third area, located behind the blue one, is white-grayish (as the ciliary muscle is visualized by transparency) and triangular, and made up of scleral tissue covering the external surface of the ciliary muscle.

Figure 3 includes figure 2 at its center and on the right, and a photograph of the surgery when the second triangular scleral flap is removed, has been placed on the left. On this flap removed, the hazel- or

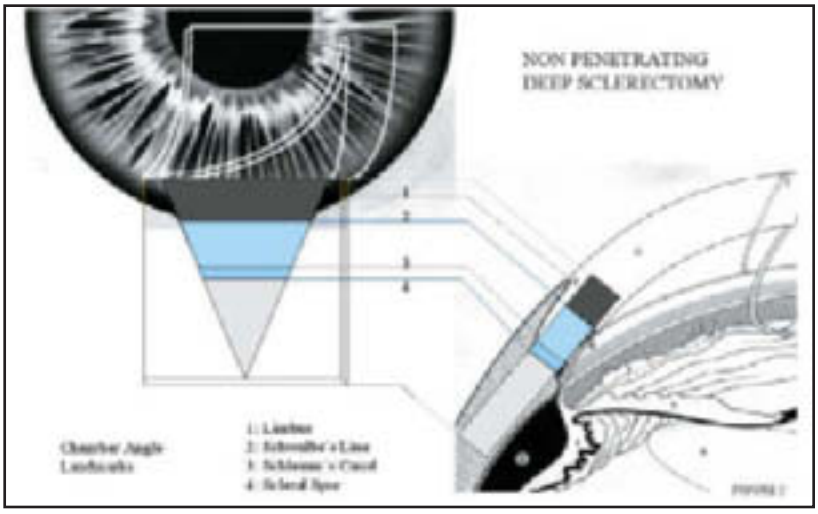


Figure 2: The dissection has been correctly performed if three clear areas are visualized. Dark area (limbar area). Blue area 2 (more posterior), with its anterior limit corresponding to Schwalbe's line, and its posterior limit, to the scleral spur and the open Schlemm's canal. White-grayish area 3 (behind the blue area), triangular, made up of scleral tissue and covering the external surface of the ciliary muscle. On the right side of this figure the correspondence of the surgical appearance of the three areas with the anatomic elements of the chamber angle can be seen.

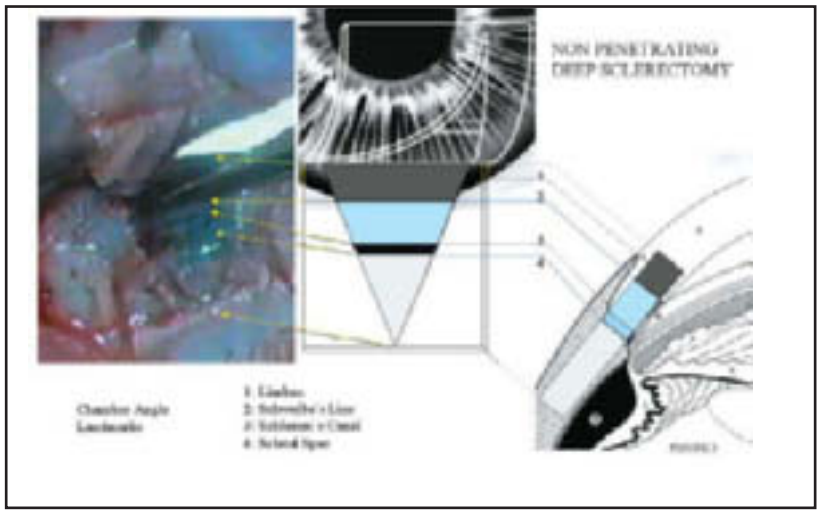


Figure 3: Removal of the second triangular scleral flap (left), on which the external wall of Schlemm's canal, identified by its hazel- or brown-colored granulous appearance, can be seen. Center and right: correlation of this photograph with the landmarks of figure 2.

brown-colored granulous sector observed is the external wall of Schlemm's canal, from which some drops of aqueous humor are seen flowing smoothly.

The anatomo-pathologic examination of the triangular flap resected shows some corneal lamellae and the endothelium of the external wall of Schlemm's canal (fig. 4 a). The flat preparation of figure 4 b shows the endothelial nuclei of the external wall of Schlemm's canal.

If the dissection has failed to be done at the correct plane and it is not deep enough for the resection of the external wall of Schlemm's canal by means of the triangular flap, the image of figure 5 will be seen, i.e., the dark area 1, the blue area 2 and the grayish-white area 3; moreover, the open Schlemm's canal will not be seen in area 2, light blue. Should this happen, special attention should be given to the blue area, and the fact that Schwalbe's line is the anterior limit and the scleral spur is the

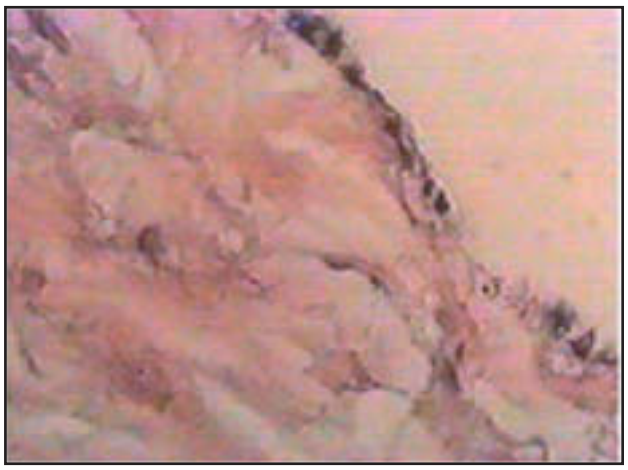


Figure 4 a: Anatomo-pathologic examination of the triangular flap showing some corneal lamellae and the endothelium of the external wall of Schlemm's canal.

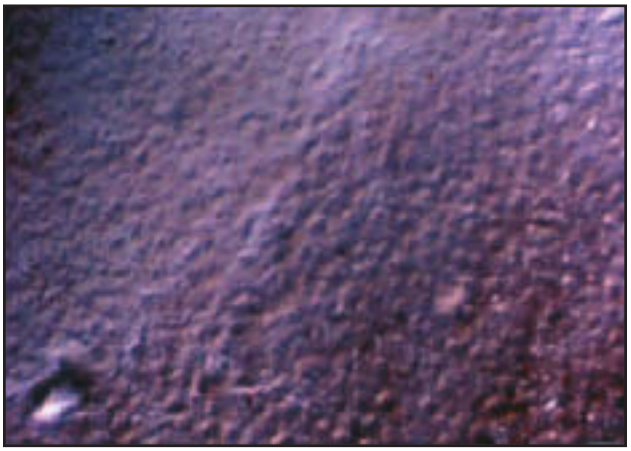


Figure 4 b: Endothelial nuclei of the external wall of Schlemm's canal (flat preparation).

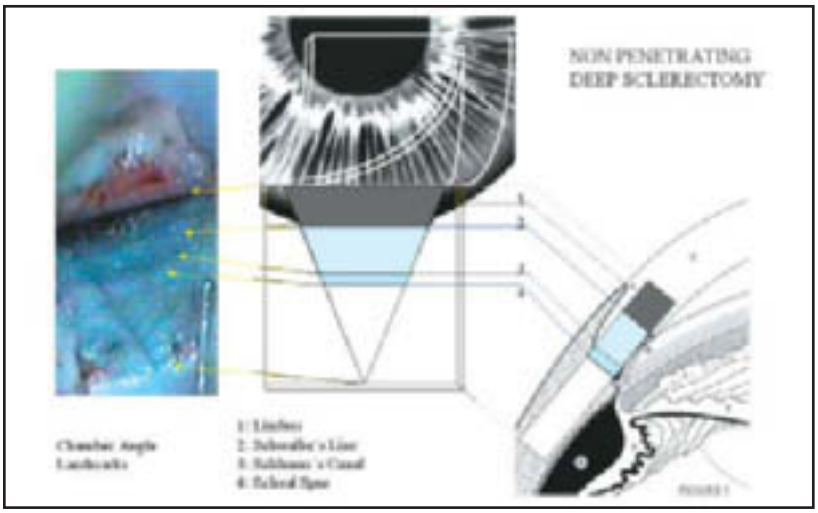


Figure 5: Image visualized if the dissection has failed to be done at the correct plane and it is not deep enough for the resection of the external wall of the Schlemm's canal by means of the triangular flap. All three areas are visible but the open Schlemm's canal is not (left). The schematic representation at the center shows the key element for the surgeon to find the Schlemm's canal: the most posterior darker blue sector (between 3 and 4) of the blue area corresponds to the Schlemm's canal.

posterior one should be taken into account. The external wall of Schlemm's canal, located **at the darkest blue area adjacent to the posterior line of the blue area (scleral spur)** (fig 6) should thus be dissected with fine clamps and with a sharp knife. Then, some aqueous humor drops will smoothly come out. Adjacent to the scleral spur (number 4 in the figure), there is a definite darker area, also blue, corresponding to the Schlemm's canal and represented in the figure by number 3.

Figures 7 A and B illustrate the dissection of the external wall of Schlemm's canal under direct illumination (a) and under transillumination (b), done with an instrument specially designed for this purpose by Grieshaber.

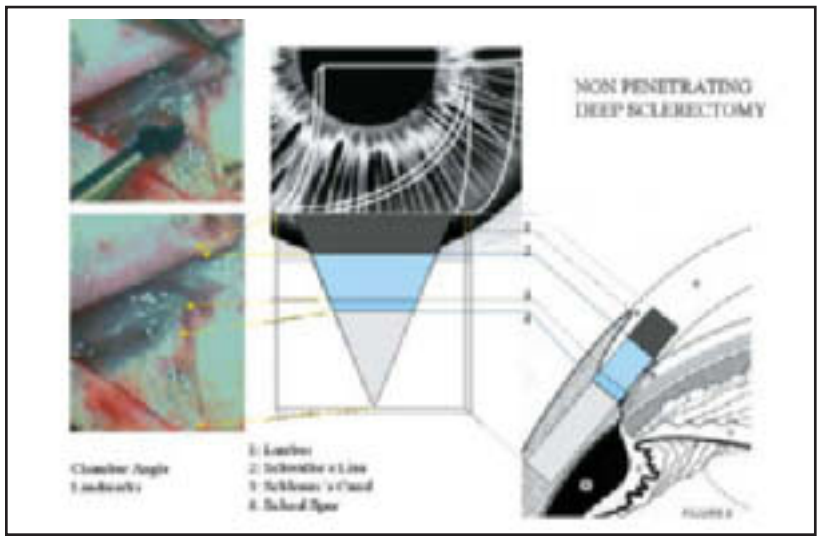


Figure 6: The most important surgical step is to open Schlemm's canal, located at the posterior part of the blue area, adjacent to the scleral spur.

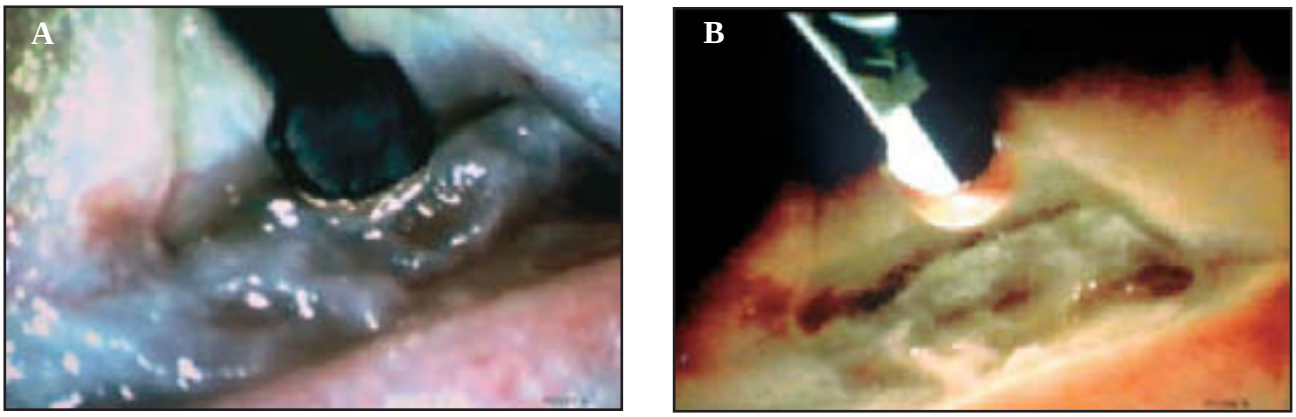


Figure 7: Dissection of the external wall of the Schlemm's canal under direct illumination (a) and under transillumination (b), done with an instrument specially designed for this purpose by Grieshaber.

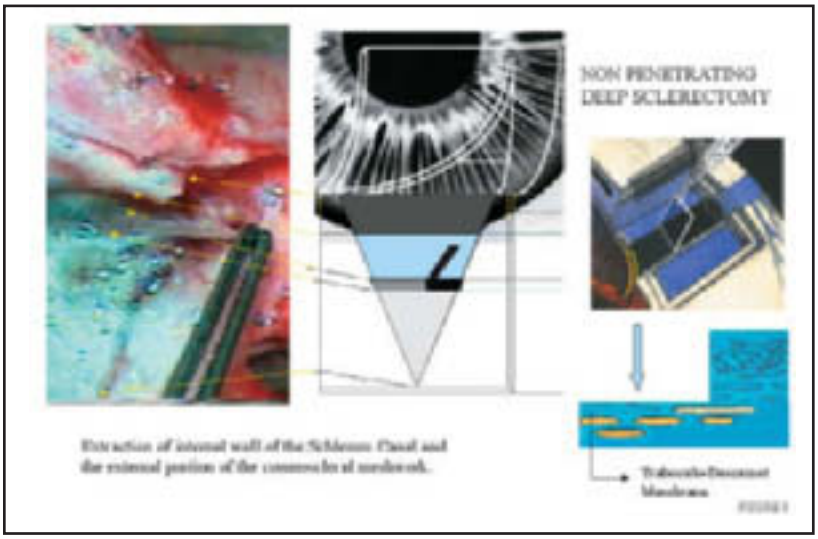


Figure 8: dissection of the inner wall of Schlemm's canal with its endothelium, juxtacanalicular tissue and the external corneoscleral trabecular meshwork (left). Schematic representation of the tissue removed and of its previous locations (center), where only the internal corneoscleral trabecular meshwork and the uveal trabecular meshwork, which, together with Descemet's membrane form the trabeculo-descemet's membrane, are left (bottom-right).

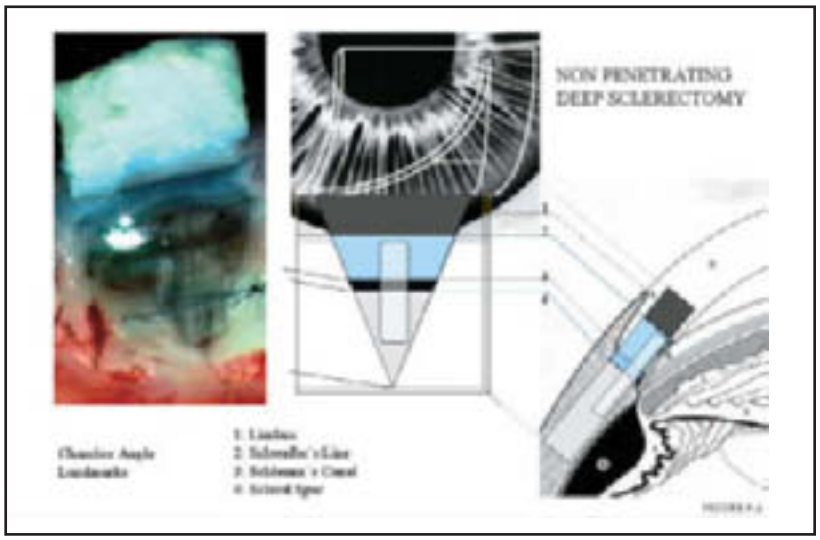


Figure 9a: Correctly placed implant (Staar) (photograph taken during the surgical procedure).

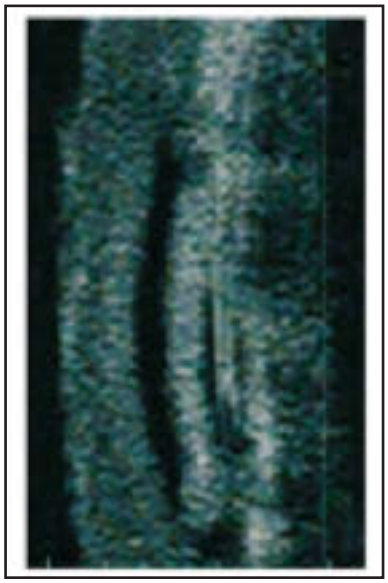


Figure 9b: Ultrasound biomicroscopy showing, from left to right: conjunctival tissue with aqueous humor, separating it from the cuadrangular scleral flap and two parallel lines behind it corresponding to the implant, where the nylon suture securing it can be seen. The implant is surrounded by aqueous humor and the scleral lake is seen behind it.

Figure 8 shows the dissection of the internal wall of Schlemm's canal with its endothelium, juxtacanalicular tissue and the external corneoscleral trabecular meshwork. On the right-bottom there is a schematic representation of the tissue removed and of its previous locations, where only the internal corneoscleral trabecular meshwork and the uveal trabecular meshwork, which, together with Descemet's membrane form the trabeculo-descemet's membrane, are left.

Figure 9a is a photograph taken during the surgical procedure showing the implant (Staar) correctly placed and secured with a nylon 10/0 suture. Correct placement of the implant can be verified by ultrasound biomicroscopy (figure 9b).

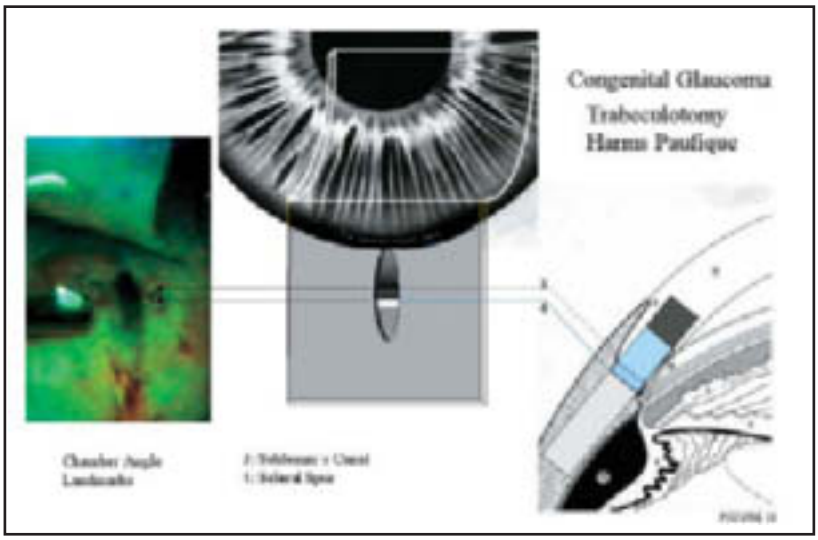


Figure 10: Same correlation with Harms and Paufique's trabeculotomy technique. The most important element to be identified is the scleral spur. After creating the cuadrangular flap by which the scleral thickness is reduced, an incision is performed perpendicular to the limbus. When this incision is open, a black triangle is visible beside the limbus, followed by a gray-nacreous triangle, on the vertix of which there is a white-nacreous area corresponding to the scleral spur (4). The trabeculotome is introduced parallel to the limbus in the dark triangle, adjacent to the scleral spur. Left: photograph taken during the procedure. Right: anatomic correlation.

This correlation was the same when we used Harms and Paufique's trabeculotomy technique (figure 10). After creating the square scleral flap, when we opened the incision performed perpendicular to the limbus in order to find Schlemm's canal, a superior dark triangle corresponding to the lumen of the open Schlemm's canal and an inferior whitish triangle corresponding to the sclera covering the anterior surface of the ciliary muscle, could be seen through the oval thus created. A white-nacreous line corresponding to the circular fibers of the scleral spur was also seen between both triangles. The trabeculotome is introduced in the superior triangle, first on the right and then on the left, in order to perform the trabeculotomy.

In children, if the procedure has been done properly, a little hyphema reaching out to the pupil but not surpassing its borders should be seen (fig. 11). This hyphema is caused by the rupture of the artery of Schlemm's canal, which is known as Friedenwald's artery. Should a large hyphema filling the whole anterior chamber develop, it would indicate that a cyclodyalisis has been done instead of a trabeculotomy.

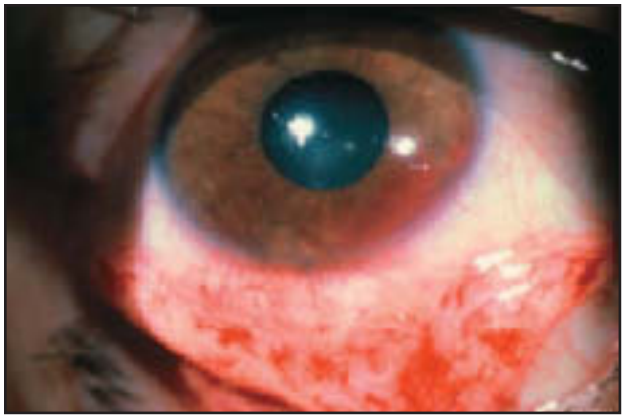
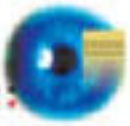


Figure 11: Very small hyphema extending to but not surpassing the pupillary border. This may occur in children after trabeculotomy, if the procedure has been done correctly.



Upon gonioscopy performed 1 week after trabeculotomy, blood is seen coming from the Schlemm's canal to the anterior chamber through the opening performed on the Schlemm's canal (figure 12).

Results

The intraocular pressure was successfully regulated in 85 % of cases, with 10 cases requiring Yag Laser at the level of Schwalbe's line, cornea and trabecular meshwork, according to Mermoud's technique (Mermoud et al 1999). With the addition of topical therapy with eyedrops, a success rate of 95 % was achieved.

The pre- and postoperative IOP values were 28.2 mmHg ± 7 mmHg and 13 mmHg ± 7 mmHg respectively, according to single-spot checks. In all cases in which the IOP was regulated, the daily pressure curve consistently revealed mean values not exceeding 20 mmHg and a variability (standard deviation) lower than 2.1 mmHg. The daily pressure curves performed preoperatively yielded the following overall results: Mean (M): 24 mmHg; Variability (V): 2.6 and the postoperative values were 15.8 mmHg and 2.0 respectively.

The main advantage of this technique is the high percentage of cases in which it prevents the three most severe complications of trabeculectomy: flat chamber, hyphema and choroidal detachment. Furthermore, since neither anterior chamber opening nor iridectomy or atropine instillation into the anterior chamber are required, the postoperative period is good, with the patient preserving the preoperative visual acuity, while our experience with trabeculectomy has shown us an otherwise difficult postoperative course, independently of the success of the procedure.

Moreover, the mild postoperative period, as well as the low percentage of complications has encouraged surgeons to safely recommend this technique as early as in the pre-perimetric period, when damage to the optic nerve has already occurred and pharmacotherapy has failed to regulate IOP, though visual acuity and visual field are still normal. This technique is thus pretty close to the ideal therapy for the prevention of serious anatomic and functional damage caused by the disease.

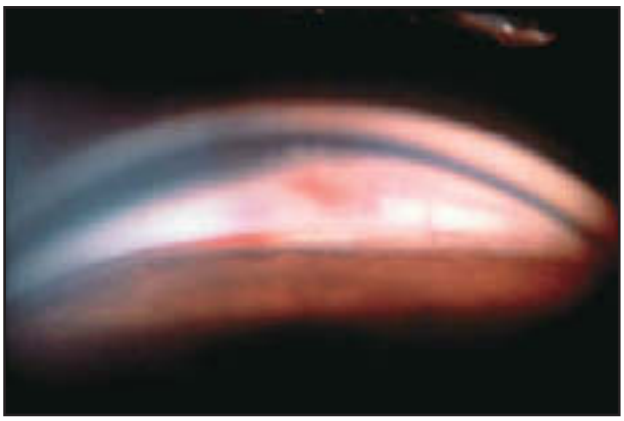


Figure 12: Postoperative gonioscopy showing blood coming from Schlemm's canal extending to the anterior chamber through the opening of Schlemm's canal.

Pathological Anatomy of the Triangular Flap Technique

Each triangular scleral flap has been studied both macro- and microscopically. The macroscopic evaluation was done according to the surface technique reported at the Microscopy Meeting of the Pathology Academy (Zarate 1999), which is based on two main principles involved in the inclusion process: firstly, transparency of the specimen after passing it through xylol and secondly, application of Scheimpflug's principle by which an excellent resolution at different planes can be obtained.

The biopsies were fixed in buffer 10 % phormol to be later dehydrated in three stages, in the first two stages in 96 % alcohol for 10 hours each and in 100 % alcohol in the last stage. Finally, they are placed in xylol for three hours. Then, when each specimen is placed on a slide, the endothelial surface should be marked as a tip for orientation upon its inclusion in paraffin. The specimen is cut by freezing and photographs are taken as necessary. A tiny cut at the vertex of the triangle located nearest to the surgeon, done with scissors during surgery upon removing the flap, is very useful for the pathologist to handle it safely.

Results

Deep sclerectomy specimens have an irregular architecture towards the edges, in contrast to those from ordinary trabeculectomies. The internal surface of the external wall of Schlemm's canal can be identified by the clearly visible nuclei of the endothelium, and pigmented areas are usually seen as well. The histologic section of figure 4a shows a dense connective tissue wall adopting a pink acidophilic color when stained with hematoxylin-eosin, as well as a sector lined with endothelial cells of an enlarged shape forming a single coat of tightly attached cells which constitutes the endothelium of the external wall of Schlemm's canal. Nuclei are typically oval-shaped and they have soft cromatin. The scleral connective tissue shows fibroblasts which are irregularly spread along the collagen. The flat preparation of figure 4 b shows the nuclei of the endothelial cells of the inner surface of Schlemm's canal.

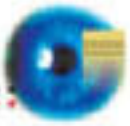
Figure 13 illustrates a flat preparation showing a collector entering Schlemm's canal.

Nd:YAG Laser Goniopuncture

In 20 % of cases, YAG goniopuncture was required between months 1 to 5 postoperatively for IOP regulation in cases reaching as high as 20 mmHg or more according to a single-spot check, or in the presence of pathologic results revealed by a daily pressure curve. The lens designed by Rousell and Fankhauser and manufactured by Haag Streit was used for this procedure. The aim was to perforate the resistance zone if surgery had failed to remove part of the corresponding tissue, and thereby communicate the anterior chamber with the scleral lake or the



Figure 13: Flat preparation showing a collector coming into the Schlemm's canal.



subconjunctival space. The aiming beam is focused on the trabeculo-descemet's membrane with a power of 2 to 3.5 mJ; however, sometimes, higher power, 4 to 5 mJ is required, but it should be kept in mind that a power above 4 mJ may cause small hemorrhages which can be stopped by strongly pressing the lens against the eye. A total of 5 to 20 shots should be made at the level of Schwalbe's line, as well as above and below it. Digital massage, which is usually indicated after trabeculectomy, is wholly contraindicated in these cases. However, more experienced surgeons have now concluded this YAG goniopuncture to be necessary in 48 % of cases (Mermoud 2001).

Chamber Angle and Non-Penetrating Deep Sclerectomy

The chamber angle is a key factor when making the decision whether to perform NPDS, since this procedure is contraindicated in narrow-angle or angle-closure glaucomas, as it is in neovascular glaucomas, in cases with newly-formed membranes covering the trabecular meshwork zone after some trabeculoplasty procedures (Sampaolesi 1991 and Koller et al, 1995) and in congenital glaucomas with both types of angles: type I: pathological mesodermal remnants reaching out to or surpassing Schwalbe's line, and type II: apparent high insertion of the iris (Sampaolesi 1997 and 1998).

This procedure is suitably indicated in primary open-angle glaucoma, capsular glaucoma, pigmentary glaucoma, traumatic glaucoma, etc. It has been widely accepted that 40 % of cases of POAG in young patients (30 to 50 years of age) have goniodysgenesis characterized by the presence of pathological mesodermal remnants (Kniestedt, Gloor et al, 2000). These remnants may reach as far as the spur, the trabecular meshwork or Schwalbe's line. This is associated with a peripherally atrophic iris mesodermal superficial layer with black triangles visible at its periphery (pigmentary layer) formed between the radial vascular cords. The radial vessels and the iris greater arterial circle are also seen. Additionally, there is absence of ciliary body band, which is covered by pathological mesodermal remnants.

However, NPDS is indicated in these cases when the pathological mesodermal remnants do not surpass the scleral spur.

Figure 14a shows a case of glaucoma with exfoliation syndrome where there is the typical wave-like pigment line on the posterior surface of the cornea (Sampaolesi's line) at the sloping part of the



Figure 14 a: Glaucoma with Exfoliation Syndrome

The typical wave-like pigment line on the posterior surface of the cornea (1-Sampaolesi's line) at the sloping part of the chamber angle between 3 and 9 o'clock, going through the 6 o'clock position in a case of glaucoma with exfoliation syndrome.

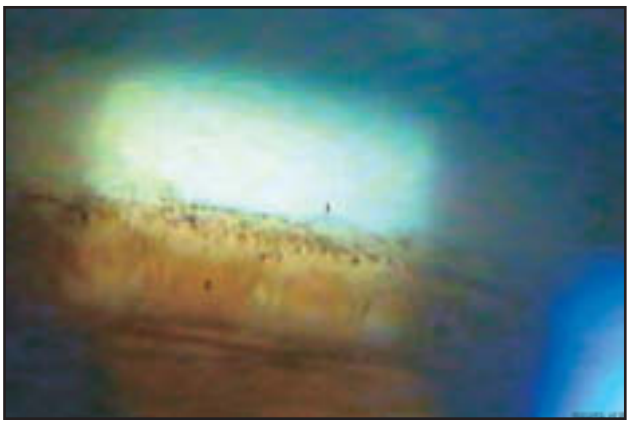


Figure 14 b: Exfoliation syndrome with mesodermal dysgenesis.

chamber angle between 3 and 9 o'clock, going through the 6 o'clock position. This sign is important for early diagnosis of the syndrome before the typical signs develop on the pupil. In a population of 110 cases (Sampaolesi, 1959), 62 had the classical signs, whereas 50 cases were diagnosed based only on the presence of the typical waves, though the classical signs were absent. According to Mizuno (1977), Sampaolesi's line is observed in 94 % of cases presenting with the typical signs and in 82 % of those in which these signs are absent. Figure 14b illustrates an exfoliation syndrome case with mesodermal dysgenesis. Pigmentary glaucoma is a late congenital glaucoma (Malbran, 1957) and it is therefore associated with goniodysgenesis. Figure 15a shows the typical image of a very dark, almost black, Schlemm's canal (1 in the figure), absent ciliary body band, which is covered with pathological mesodermal remnants (2), peripheral atrophy of the superficial mesodermal layer of the iris (2 to 4) by which the dark triangles corresponding to the pigmentary epithelium (3) become visible, and vascular cords with radial vessels (4). These last features are typical in goniodysgenesis. Figure 15b shows another case

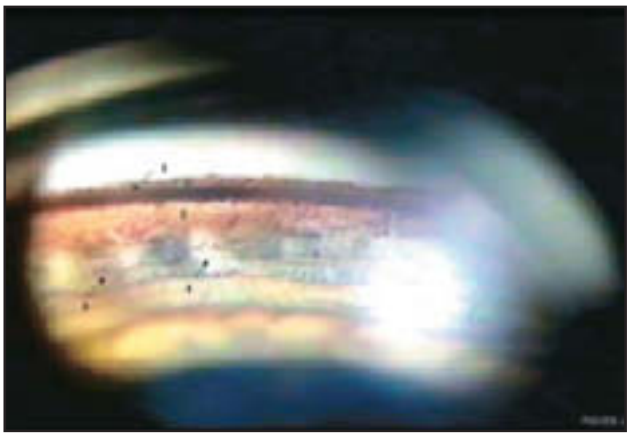


Figure 15 a: Goniodysgenesis

Very dark, almost black, Schlemm's canal (1), absent ciliary body band, which is covered with pathological mesodermal remnants (2), peripheral atrophy of the superficial mesodermal layer of the iris (2 to 4) by which the dark triangles corresponding to the pigmentary epithelium (3) become visible, and vascular cords with radial vessels (4). These last features are typical in goniodysgenesis.

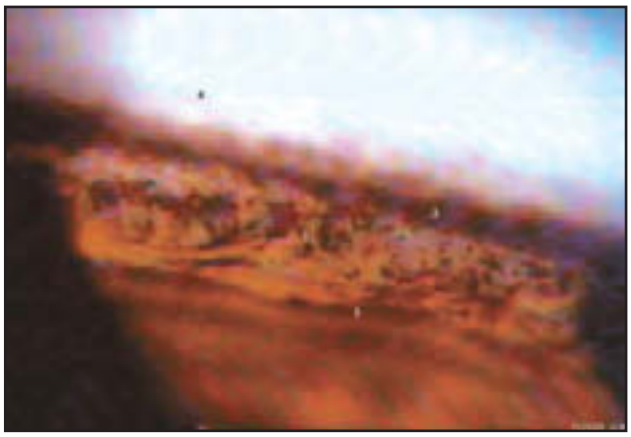


Figure 15 b: Another case where the iris atrophy is not marked, while the presence of very thick pathological mesodermal remnants (1), covering the ciliary body band, is clearly visible. 2: last iris roll, 3: highly pigmented Schlemm's canal, 4: Schwalbe's line.

where the iris atrophy is not marked, while the presence of very thick pathological mesodermal remnants (1), covering the ciliary body band, is clearly visible. The last iris roll is indicated with number 2, the highly pigmented Schlemm's canal, with number 3, and Schwalbe's line, with number 4.

Figure 16 shows a goniodysgenesis, without pigmentary glaucoma, where the pathological mesodermal remnants cover the ciliary body band completely.

Gonioscopy after Non-Penetrating Deep Sclerectomy

Figures 17 a and b illustrate the typical appearance of the chamber angle after NPDS. The dark area (a) on the external wall of the chamber angle is the scleral lake (1 in the figure), which can be clearly seen full of liquid with a fine slit cut (b).



Figure 16: Goniodysgenesis without pigmentary glaucoma. The pathological mesodermal remnants cover the ciliary body band completely.





Figures 17: Typical appearance of the chamber angle after NPDS. The Schlemm's canal and the trabecular meshwork have become convex, raised towards the interior of the anterior chamber, because they have been displaced by the cylindrical implant, which deforms them. In a, the dark area seen by difuse illumination on the external wall of the chamber angle is the scleral lake (1), which, in b, it is seen full of liquid with a fine slit cut.

Both figures show the Schlemm's canal and the trabecular meshwork which have become convex, raised towards the interior of the anterior chamber, because they have been displaced, and therefore, deformed, by the cylindrical implant.

Figures 18 a and b show another appearance of the chamber angle after this procedure. In a it looks as if the procedure has been penetrating, however, if viewed in a fine slit cut (b), a very thin trabeculo-descemet's membrane is seen.

Figure 19 shows the accidental perforation of the trabeculo-descemet's membrane during the procedure.

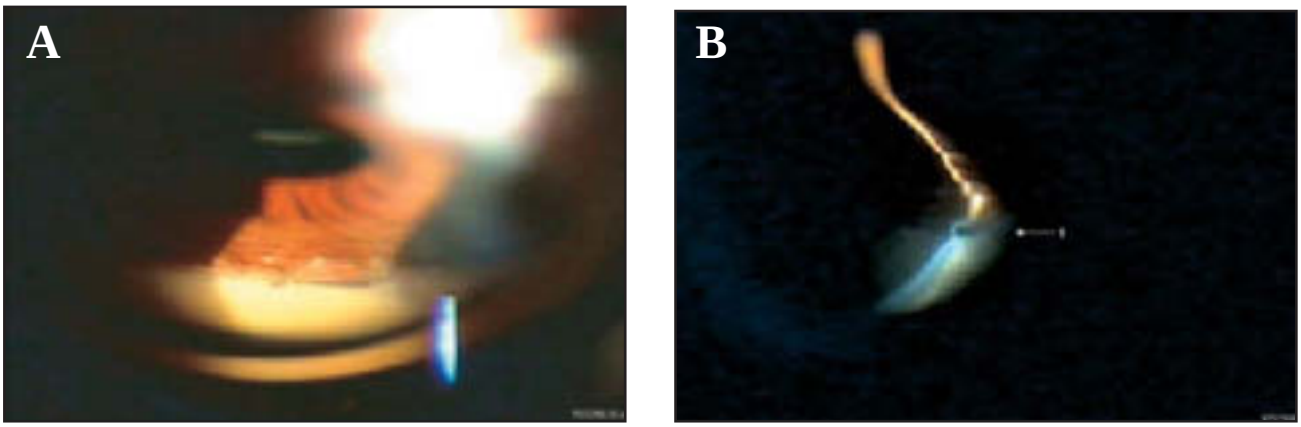


Figure 18: Another appearance of the chamber angle after this procedure. In (a) it looks as if the procedure has been penetrating, however, if viewed in a fine slit cut (b), a very thin trabeculo-descemet's membrane is seen.

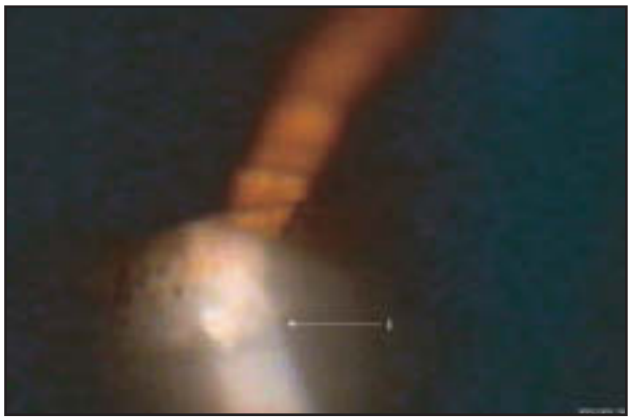


Figure 19: Accidental perforation of the trabeculo-descemet's membrane during the procedure.



Figure 20: Absence of the uveal trabecular meshwork, of the external corneoscleral trabecular meshwork and of the juxtacanalicular tissue after a Yag-laser procedure. This area is limited by two white cords: Schwalbe's line (1) and scleral spur (2) and it is usually filled with blood (3), which comes into the anterior chamber, as it occurs in congenital glaucomas after trabeculotomy. Bleeding is stopped by slightly pressing the lens.

Figure 20 shows the absence of the uveal trabecular meshwork, of the external corneoscleral trabecular meshwork and of the juxtacanalicular tissue after a Yag-laser procedure. This area is limited by two white cords: Schwalbe's line (1) and scleral spur (2) and it is usually filled with blood (3), which comes into the anterior chamber, as it occurs in congenital glaucomas after trabeculotomy. Bleeding is stopped by slightly pressing the lens.

Other Non-Penetrating Procedures

In addition to NPDS, other techniques have been used and, though considered to be non-penetrating, they sometimes feature small perforations, such as Stegmann's viscocanalostomy (Figure 21). The first steps of this technique are the same as those for NPDS, but the external wall of Schlemm's canal is removed with the second flap, while the inner wall is left intact. Viscoelastic substance, which is then injected through both orifices of Schlemm's canal, clears the aqueous humor outflow pathways from Schlemm's canal onwards. Anatomo-pathologic studies performed by Johnson and Johnson (2000) on human eyes after viscocanalostomy revealed that the external wall of Schlemm's canal was open at the area closest to Schwalbe's line.

In another technique created by Burk, Hydrotrabeculotomy (Figure 22), the first steps are also the same as in NPDS, but, a channeled Geuder

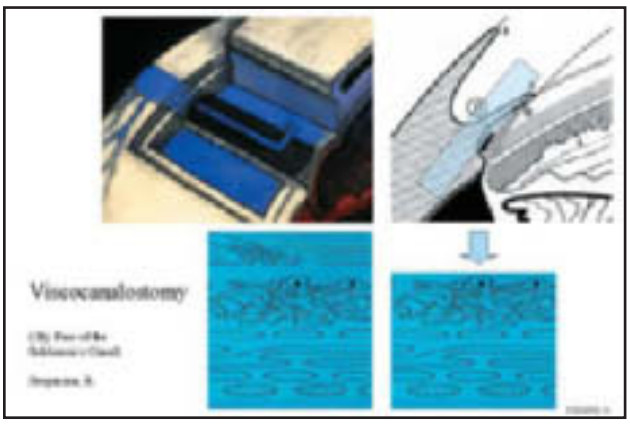


Figure 21: Stegmann's viscocanalostomy.

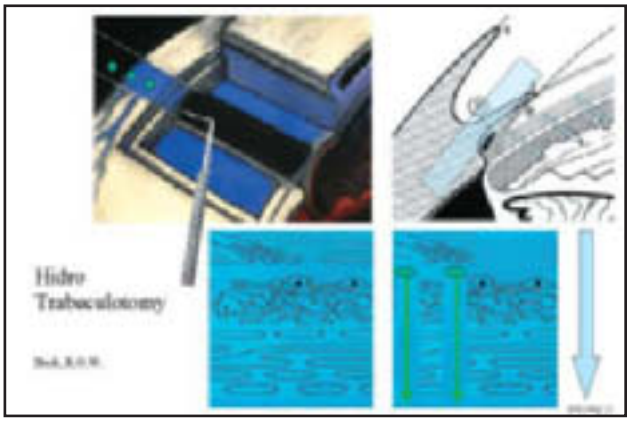


Figure 22: Hydrotrabeculotomy.

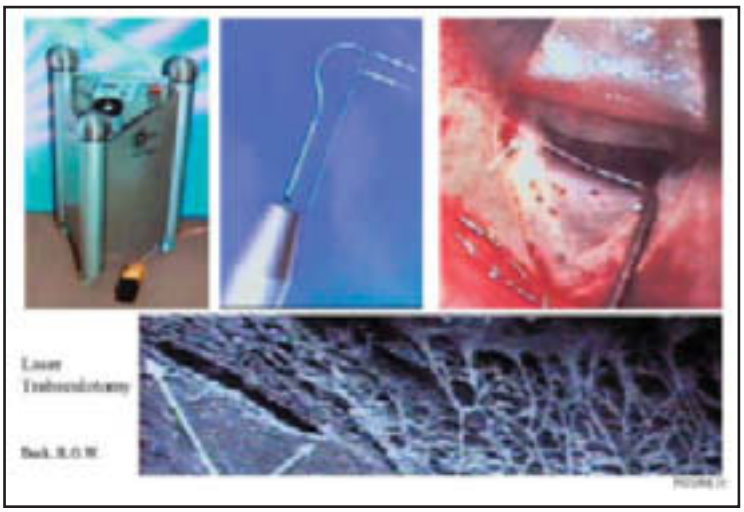


Figure 23: Laser trabeculotomy.

trabeculotome through which serum can be introduced by pressure, perforates the inner wall of Schlemm's canal and the trabecular meshwork, thus penetrating into the anterior chamber. This technique is actually perforating, although the anterior chamber is not emptied. When we used this technique, a small intraoperative hyphema not reaching the pupil was observed, which was produced by the rupture of the artery of Friedenwald, as shown by figure 11 (Burk, 2001 [paper]).

Burk also has recently presented laser trabeculotomy (figure 23) (Burk, 2001, [poster]). The laser rays emitted towards the anterior chamber by a small gold angled mirror attached to the trabeculotome perforate the inner wall of the Schlemm's canal and the trabecular meshwork up to the chamber angle, as seen in the scanning electron microscopy at the bottom of the figure (white arrows).

Discussion

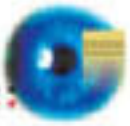
Non-penetrating deep sclerectomy, provided that the technique is properly performed, by carefully observing the morphology of the external wall of the chamber angle and establishing the right correlation between the elements of the external wall of the chamber angle at the three zones visualized by the surgeon after the dissection of the deep triangular flap, should lead to the successful removal of the external wall of Schlemm's canal as well as its inner wall with the juxtacanalicular tissue and the external corneoscleral meshwork.

Throughout our short experience of five years, this new technique has proven to be equally effective in IOP regulation as trabeculectomy.

By postoperative ultrasound biomicroscopic examination correct placement of the implant is verified. This technique also reveals the presence of aqueous humor in the subscleral lake and, in some cases, its outflow through the unconventional uveoscleral pathway (figure 9b).

The typical complications of trabeculectomy, such as athalamia, hyphema and choroidal detachment, have barely occurred. Moreover, and among the advantages of this technique, the fact that no anterior chamber opening, iridectomy or use of mydriatics are required, as well as the good evolution, with recovery of the preoperative visual acuity as early as on the first postoperative day, should be mentioned.

Its safety and immediate good postoperative evolution warrant the indication of surgery as early as in the pre-perimetric period of glaucoma, when medication fails to regulate the IOP and in the presence of optic nerve damage as revealed by the HRT, when both visual acuity and visual field are normal, thus becoming a useful and more efficient tool which can help glaucomatous patients prevent the serious damage caused by this disease to the optic nerve, and, consequently, to the visual field.



Acknowledgment

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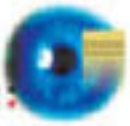
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Chapter 25
FILTERING GLAUCOMA SURGERY WITH EXCIMER LASER

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Arturo Maldonado-Junyent, M.D.

What is LTA? How Does it Function?

The laser trabecular ablation (LTA) is a new, non-penetrating filtering operation for the treatment of open angle glaucoma.

Excimer ablation appears to be an effective option for the treatment of glaucoma as demonstrated in 57 eyes operated for open angle and pseudo exfoliative and pigmentary glaucoma, with an average follow-up of 869 days with 56 days minimum and a maximum of 1580 days. For many surgeons, it is also a simpler procedure than other non-penetrating filtering procedures.

The surgical procedure involves: topical anesthesia, conjunctival incision, lamellar scleral flap, ablation of the roof and inner wall of Schlemm's canal together with part of the yuxta-canalicular meshwork and partial ablation of the trabeculum, utilizing a scanning or diaphragm excimer laser system until a microperforation is produced in the underlying corneo-trabecular tissue. The microperforation does not convert this into a functionally perforating procedure as it has no positive or negative effect on the treatment - it is merely used as a sign that the ablation is deep enough and that consequently it should be stopped.

The scleral flap and conjunctiva are sutured. No antimetabolites are used.

This operation is based on combining Arenas Archilla's[1] concept of the extirpation of Schlemm's canal and part of the trabeculum under a scleral flap, using an excimer laser as described by Seiler[2]. This produces a lake of subscleral filtration, as in lamellar techniques such as deep sclerectomy, without making a functional opening into the anterior chamber.

A prospective study has been done to test whether our clinical impression of the efficacy of this procedure was correct, and to evaluate its failure rate and complications. This procedure is a functionally non-invasive surgery with excimer ablation of adjacent sclera, Schlemm's canal and the juxta-canalicular trabeculum. This allows the aqueous humor from the anterior chamber filter towards the subscleral space through the deep thin remaining layers of trabeculum.

The average presurgical intraocular pressure in this series was 28.40 mm Hg, SD +/- 8.89; postsurgical 13.30 mm Hg, SD 2.92. The average reduction in the IOP was 14.93 mm Hg SD +/- 9.19 (52.17%).

Methods

Between May 1997 and July, 57 consecutive eyes with open angle, pseudoexfoliative and pigmentary glaucoma were operated. The average age of the patients was 58.09 years with a range of 17 to 79. There were 32 males (56.14%) and 25 females (43.86%).

Because of the high presurgical intraocular pressures, leaving a control series of these patients untreated was felt to be both unethical and unneeded. For such reason, in the same period, 197 eyes were operated in other patients with a classic trabulectomy or deep sclerectomy.

Previous glaucoma treatment in the series included topical betablockers, pilocarpine, sympathomimetics, and oral acetazolamide.

Preoperative medications used were antibiotics (erythromicin and ciprofloxacin) given 48 hours prior to surgery, combined with topical steroids and flubiprofen drops every 6 hours. Parenteral aminoglucosides, Amikacyn 500 mg, were administered every 12 hours, for 24 hours before and after surgery. The eyedrops were continued for 7 days, every 6 hours, and then for another 7 days every 12 hours.

Surgical Technique

Topical anesthesia is used with proparacaine 0.5 % and lidocaine 4 %, one drop every five minutes for half an hour before surgery. The procedure begins with an optional paracentesis (small penetrating corneal incision).

A fornix conjunctival incision is performed, dissecting Tenon's capsule. Hemostasia is made with bipolar diathermy, using minimum intensity.
Although the scleral incision may have a rectangular, round or oval shape as in conventional procedures, (optional for the surgeon) the cut is more tidily performed with a circle straddling the limbus previously marked with the help of a 4.25 mm optic zone marker (Fig. 1).

With a radial keratotomy diamond knife calibrated at 350 microns, the corneo scleral incision is performed beginning in the cornea and proceeding in a semicircle in the sclera, back into the cornea again (Fig. 2). This step secures uniformity in the depth of the incision and consequently in the thickness of the scleral flap obtained. This will make the laser ablation more uniform.

Once the flap is dissected and bent forward over the clear cornea to expose the area that will be

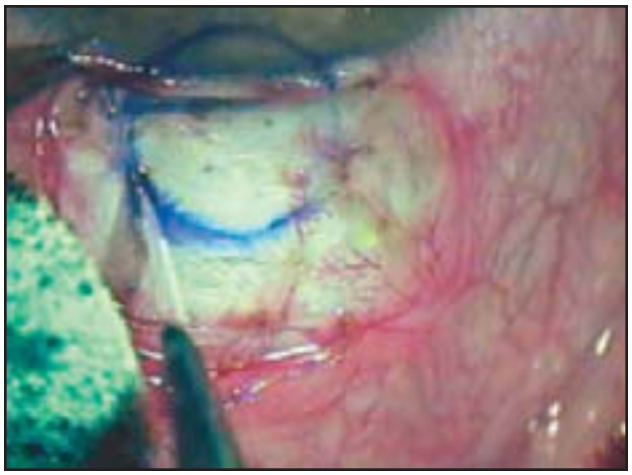


Fig. 1. Performing the Scleral Incision.
Once the fornix conjunctival incision is performed, a round sclerectomy dissection is done. The area is previously marked with the help of a 4.25 mm optical marker zone.



Fig. 2. Deep into the Sclera.
With the diamond knife a corneo-scleral incision is made (approximately 350 microns depth) and proceeding back to the cornea again.

treated, a mask, specially designed with a 2 x 4 mm window, is placed to protect the surrounding tissue from the excimer rays (Fig. 3).

The ablation of the deep scleral wall is made using PTK software that removes successive layers of 0.25 (Summit SVS Apex Plus) to 2 microns (Lasersight 200 minicompact and Lasersight SLX) in thickness. With the Summit, the ablation takes 3 minutes and with Lasersight approximately 6 minutes (Fig. 4).

This allows a progressive, controlled thinning of the exposed deep scleral cornea tissue to reach Schlemm's canal, and its roof and part of its internal wall is then ablated, followed by partial ablation of the trabecular meshwork and the adjacent corneal stroma 1 millimeter in front of the Schlemm's canal. Excimer ablation is continued up to the moment when a drop of aqueous humor appears, signalling a microperforation of the adjacent Descemet's membrane.

The first eyes were operated in 1997, using Lasersight in 9 of these cases and Summit in one case. Since the technique was new, different variations were tried, such as stopping the lathing when the filtration started from the Sclemm´s meshwork in one case, making microperforations with and without iridectomy, trying to define where the limit of the ablation should be. It was shown that it was sufficient to ablate until a microperforation was produced. The progress of the eyes treated was observed, and only after 6 months (October 1997 to April 1998) had shown the effectiveness of the treatment, was the series re-started.

In cases with a shallow anterior chamber, an iridectomy can be performed by drying the surface of the trabeculum and continuing the excimer ablation to produce a true perforation. The gush of the aqueous draws the iris root against or into the perforation. This allows the surgeon to perform a manual iridectomy or to make an iridotomy with the excimer beam. The iridotomy may be performed instead as a secondary procedure with a Yag laser.

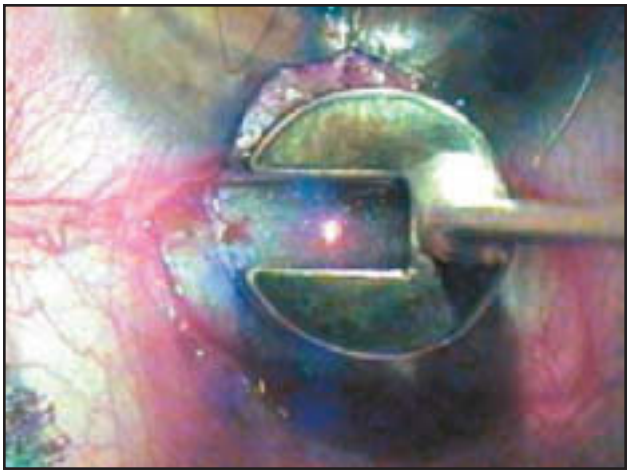


Fig. 3. Preparing the Exposed Area for Ablation.

Once the flap is dissected and forward over the clear cornea, a metallic mask, specially designed is placed to protect the surrounding tissues during the ablation with the excimer laser.

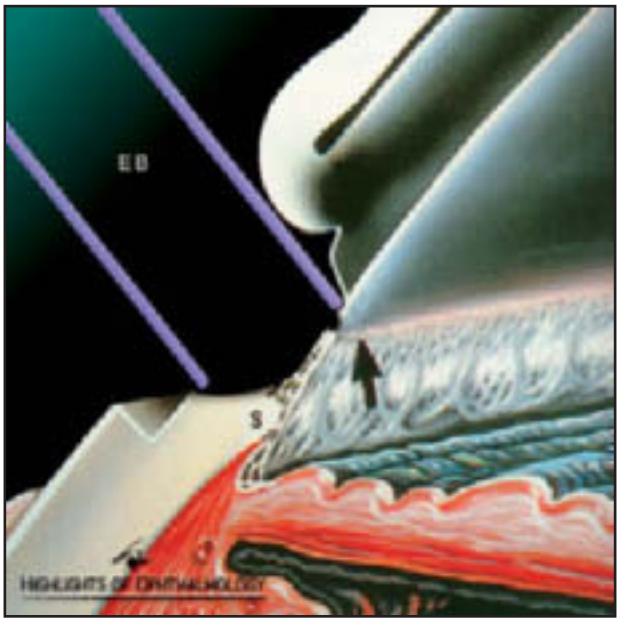


Fig. 4. Non-Penetrating Filtering Operation with Excimer Laser

EB represents the excimer beam acting over the ablated zone. S (Schlemm's canal) has been unroofed and the trabeculum partially ablated in the anterior area. There is a microperforation in the underlying trabeculum but this does not make of this procedure a penetrating filtering operation.

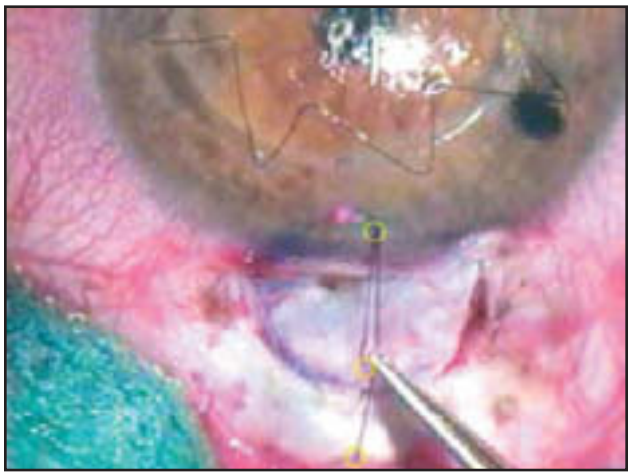


Fig. 5. Closing the Scleral Flap.
When the treatment has been accomplished, the scleral flap is repositioned and sutured with 10-0 nylon. The conjunctiva is also repositioned with two stitches anchored to the limbal episclera.

When all this has been accomplished, the scleral flap is repositioned and sutured with 10-0 nylon (Fig. 5). This suture joins the cornea, the distal edge of the flap and sclera, and may be removed during the early postoperative stage to reopen the borders of the scleral flap and so improve filtration if necessary. Sometimes it loosens spontaneously.

The conjunctiva is repositioned and sutured with two stitches anchored to the limbal episclera. Antimetabolites, such as 5-FU or mitomycin, are not used. No viscoelastic or equivalent substance is necessary in order to maintain the subscleral space.

Evaluation of Results

The results we obtained are consistent clinically and are statistically significant. The specific results of intraocular pressure have already been outlined. They are better or at least similar to those obtained with conventional procedures[3]. There are a significant number of advantages to this new approach, especially the low rate of complications, the control of pressure usually without additional medical treatment, and that the technique is easily reproducible.

Advantages

The use of this surgical technique provides a number of important advantages:

1- It allows extraocular surgery to be performed, except for a tiny microperforation, thus preventing decompression of the anterior chamber and its consequent effects.
2- It leaves an efficient intrascleral drainage as a result of a perfectly controlled LTA, owing to the precision of the ablation performed by the excimer. This provides a technique which is reproducible for a greater number of surgeons.
3- Iridectomy is performed, when needed.
4- It creates a new indication, mechanical intrascleral filtration, for the use of the excimer laser.
5- The procedure can be performed with topical anaesthesia.
6- The corneal flap-scleral stitch allows a transitory closure of the lamellar sclerectomy to prevent a shallow chamber should there be excess filtration.

Complications

Complications are seldom found. In our series of 57 eyes we found: Hyphema 3 eyes (5.26%); choroidal detachment 5 eyes (8.77%). Posterior synechia: 1 eye (1.75%); and posterior synechia and cataract: 1 eye (1.75%), which later underwent phacoemulsification with lens implantation. From the series of 57, one eye was not controlled (IOP).

Postoperative Clinical Findings

The following changes were found on gonioscopy: a depigmented and more transparent trabecular band (Fig. 6). No presence of holes in Descemet membrane. The Ultrasound biomicroscopy showed a subscleral lake of aqueous filtration (Fig. 7).

The unroofed Schlemm's canal and the scleral spur behind it, can be seen after an experimental LTA in a cadaver eye. The histopathologic study confirms the structural anatomic changes created with surgery. (O. Croxatto -Fundación Oftalmológica Argentina).

Historical Considerations of Particular Importance

The Evolution of Concepts in Glaucoma Surgery

Goldman[4] was the first, between 1946 and 1949, to do precise experiments to determine the origin of the resistance to the outflow of aqueous humor, and identified that place as the trabeculum. Between 1955 and 1958, Grant[4] performed perfusion experiments in enucleated human eyes. Maintaining a continuous flow in the anterior chamber, he extirpated the trabeculum at the level of Schlemm's canal for 360º and found that resistance was diminished by 75%.

In 1966, Krasnov[5][6][7] stated that more than half of the glaucomas are produced by a rise in resistance in the collector and aqueous veins in the area of Schlemm's canal. He developed the sinusotomy technique, performing a manual ablation of almost the whole thickness of the sclera in a 90º arc, through which he extirpated the external wall of Schlemm's canal. This technique was lamellar, and did not penetrate into the anterior chamber.

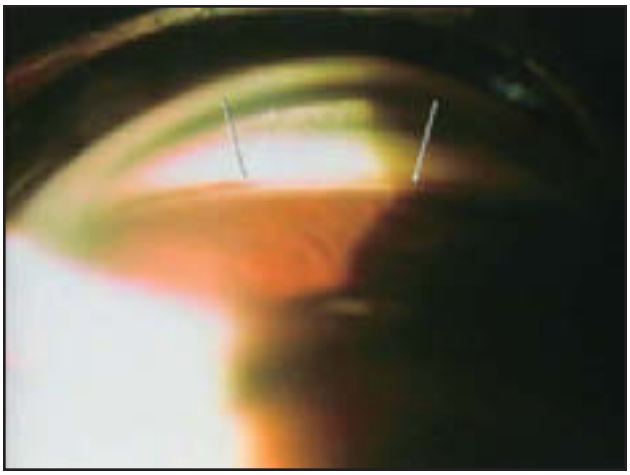


Fig. 6. Gonioscopic Configuration.
With the 3 mirror lens or the gonioscopy lens you may observe a depigmented and transparent trabecular band after the treatment (arrows).



Fig. 7. B-Scan Ultrasonic Observation.
This ultrasonic (B-scan) biomicroscopy shows a subscleral lake of aqueous filtration.

The most popular operations, however, continued to be those based on the extirpation of the full tickness eye wall including the sclera, trabeculum, Schlemm's canal and the collector channels, with subconjunctival filtration.

In 1968, Cairns[8] and Vasco Posadas[9] described a technique in which they performed a lamellar scleral flap and under it, a deep penetrating corneosclerectomy with basal iridectomy. Cairns called this a "trabeculectomy" and Vasco Posadas "protected filtration".

This technique again changed the concept of glaucoma surgery. The innovation was the combination of the extirpation of a portion of the trabeculum, Schlemm's canal and collector channels, protected by a scleral flap in order to turn the filtration into a combination of intra-scleral and subconjunctival, thus lessening the complications of the previous full thickness operations.

The Importance of Arenas' Ab-Externo Trabeculectomy

In 1993 Arenas Archilla[1] published abouter trabeculectomy, (ab-externo) which is a manual trabeculodissection. (See Chapter 21 for how this technique works. **Editor**). The concept and technique of LTA are directly derived from Arenas abexterno operation. Later on, he modified his own technique, employing a diamond drill and adding 0.04mg/cc of Mitomycin. He combined the Krasnov concepts of the manual extirpation of Schlemm's canal and part of the trabeculum, with the intrascleral protected filtration of Cairns and Vasco Posadas.

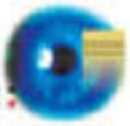
The Contributions of Viscocanalostomy

In 1999, Stegmann[10] published his technique of viscocanalostomy, in which the surgeon manually dissects a 300 micron scleral flap and another deeper one to leave a few fibers of deep sclera and Descemet's membrane free of stromal tissue. The ostium of Schlemm's canal is exposed on each side of the deep flap and a high viscosity sodium hyaluronate is introduced into the canal with a fine cannula. This encourages aqueous flow from Schlemm's canal to the aqueous veins, but probably also effects a microtrabeculotomy through the injection of the substance. (See Chapter 23 for description and illustrations of how this procedure works. **Editor**).

Stegmann also fills the subscleral space with viscoelastic substance to prevent early healing and to maintain the height of the space. Mermoud[11] places a porcine collagenous device to maintain filtration in the space. In some cases, he performs microperforation with Yag laser in Descemet's behind Schwalbe's line, to improve filtration. (See Chapter 22 for illustrated description of how this operation works. **Editor**).

Experience of Other Surgeons

Sourdille[12] extirpates Schlemm's canal manually, together with the juxta-canalicular tissue, in the belief that filtration is achieved through the thinned trabeculum as well as by the windows in the Descemet's membrane, as Stegmann states.



Sourdille[12] places a sodium hyaluronate device, which is absorbed in a few months, to maintain intra-scleral filtration.

Discussions are still continuing on whether the precise location of the resistance to filtration is at Descemet's (Stegman), or the anterior trabecular meshwork (Teichmann)[13].

Seiler[2], between 1985 and 1988, was the first to perform a partial trabeculectomy with Excimer laser. He found that 94% of the resistance was in the last 10 microns of the juxta-canalicular tissue.

There are other experiences in this field: Olander[14], Berlin[15], Takagi[16], Brooks[17], and an animal experimental model by Aron-Rosa.[18] Gimbel has performed trabecular ablations with an Excimer laser removing almost the entire scleral thickness with consequent subconjuntival filtration. (Personal communication.)

It can be concluded from the literature that all these surgical procedures tend to eliminate or reduce the resistance to the outflow of aqueous.

The glaucoma surgery most commonly employed at the moment is trabeculectomy as described by both Cairns and Vasco Posadas in 1968. (See Chapter 18 for step by step procedure of the Classic Trabeculectomy as well as the Tunnel Scleral Incision Trabeculectomy as preferred by Luntz. This is fully illustrated. **Editor**).

The disadvantage of this trabeculectomy is that the eye is abruptly decompressed when the 2.5 to 3 mm intraocular opening is made. This may result in a serious surgical accident, such as vitreous loss, and even in expulsive hemorrhage, resulting in surgical failure or even total visual loss, or in less serious post-surgical complications such as hyphema, uveitis or cataract.

Out of several different options, the most convenient procedure is to perform an ablation up to a point when a microperforation is produced. This microperforation does not imply a penetrating technique in the same way as the trabeculectomy, since it is not a functional part of the treatment, but rather the sign that the ablation is sufficiently deep and that no further ablation should be done. In fact, the iris is completely-healed after a few days.

The mechanisms of filtration should be through the conventional and also the uveoscleral way. An iridectomy is needed only in cases of narrow angle glaucoma.

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Chapter 26
LASER ASSISTED DEEP SCLERECTOMY

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Introduction

Non-penetrating filtering surgery to treat glaucoma was introduced in the 1950s by Epstein[1] and Krasnov[2] , both of whom performed a paralimbic deep sclerectomy over Schlemm's canal. They concluded the surgery by closing the conjunctiva over the thinned sclera. The initial results were good, but subconjunctival fibrosis reduced the aqueous filtration after a few months, and the IOP returned to the preoperative level. Various authors[3-8] proposed creating a scleral flap under which a deep sclerectomy was performed. The results seemed to improve, but, again, after some time there was a regression back to preoperative values. A noteworthy observation was that these non-penetrating techniques significantly reduced the complications associated with conventional full-thickness trabeculectomy.[9-15] (**Editor´s Note**: the pioneer of modern non-penetrating filtering operations was Eduardo Arenas A., who first presented his technique of trabeculectomy ab-externo in 1991, 1993, 1996. See bibliography of Chapter 20 and description in Chapter 21.)

In recent years attempts have been made to improve the long-term results using two methods. The first consisted of implanting devices under the scleral flap to reduce intrascleral fibrosis, which allows aqueous flow toward the subconjunctival space. In 1990,[8] Koslov et al. introduced a collagen implant. Sourdille[16] et al. later proposed implantation of reticulated hyaluronic acid SKGEL ®, because the slow release inside the decompression space may nourish the deprived tissues and improve their outflow functions. Some authors confirmed the results of these devices at midterm,[17-23] although data are lacking for long-term results.

The second improvements consisted of surgical modifications to the technique underwent in recent years. In 1984,[24] Fyodorov et al. proposed excision of corneal stroma behind the Descemets membrane to increase aqueous humour filtration. They then reported that the deeper tissue had to be removed, confirming the high resistance to aqueous flow of the inner layer of Schlemm's canal and juxtacanalicular trabeculum. Mermoud et al.,[18] Stegmann et al.,[26,27] and especially Sourdille et al.[16] emphasized the importance of careful dissection to selectively remove the tissues that cause high resistance, otherwise the results were worse. Stegmann et al. then proposed complementing the technique by performing a viscocanolostomy. In addition to performing a deep sclerectomy to remove

the high-resistance tissues, they injected sodium hyaluronate into Schlemm's canal using a thin cannula. This dilated the canal and prevented fibrosis formation, which facilitated aqueous outflow.[27]

Another modification of the technique is the use of a laser to ablate the sclera. Although we are aware presentations in which this idea was described, we have not found any detailed studies in the literature. The erbium YAG laser is the most commonly used to perform deep sclerectomy, and its principal purpose is to simplify surgical maneuvers. Manual scleral dissections to remove the tissue that is highly resistant to flow are complex and require training and skill. Despite a high level of surgical expertise, the sclera may be perforated, what requires converting the procedure into a full-thickness trabeculectomy. The use of the erbium:YAG (Er:YAG) laser to assist deep sclerectomy is being tested in different studies that are underway.

The aims of the present study were to determine the efficacy of erbium:YAG laser assisted deep sclerectomy to reduce intraocular pressure (IOP), the long-term results and simplify the technique. The experience we have collected in the last three years and the different studies we have performed[28-29] helped us define the surgical technique we are about to start analyzing. (**Editor´s Note**: In April 2000 at the ASCRS meeting in Boston, Dr. Arturo Maldonado B., presented his experiences with **Laser Trabecular Ablation** for non-prenetrating filtering operation using the Excimer laser. Please see Chapter 25.)

Patients and Methods

Forty-six eyes of 42 consecutive patients were studied. Patient data are shown in Table 1. Twenty-six men and 20 women, ranging in age from 27 to 68 years (average age, 62.6 ± 10.8), were included in the study. All patients had been diagnosed with glaucoma: 41 had primary open-angle

Table 1.
Preoperative patient demographic data

Nº eyes	46
N º patients	42
Female	20
Male	26
Age (years)	62.6 ± 10.8 (27 – 68)
Type of glaucoma	
POAG	41
Pigmentary glaucoma	3
Pseudoexfoliative glaucoma	2
Preoperative IOP (mm Hg)	28.3 ± 6.1
Preoperative glaucoma mediactions (29 eyes)	1.9 ± 0.7
Preoperative visual acuity	0.83 ± 0.12

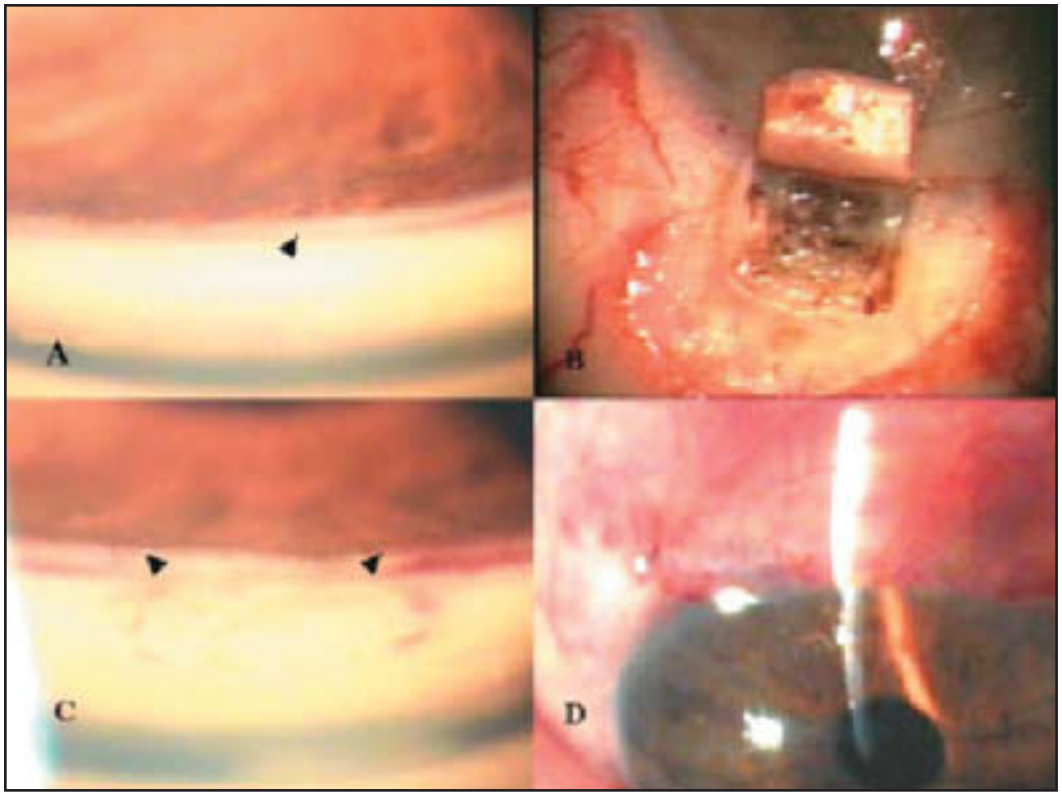


Figure 1. Gonioscopic image of Schlemm's canal (arrow) preoperatively (A). Scleral bed after erbium:YAG laser ablation (B). Postoperative image of the ablationof Schlemm's canal and the absence of blood(arrows) (C). Final postoperative result, after 24 hr, with an evident conjunctival bleb(D).

glaucoma (POAG), three pigmentary glaucoma, and two pseudoexfoliative glaucoma. All patients underwent full ophthalmologic and systemic examinations. Seventeen of the patients had never received any treatment for glaucoma, the rest were receiving topical medical treatment, all of which had POAG. Eight patients were receiving one medication, 14 two medications, and seven three medications (average number of medications, 1.9 ± 0.7). The average duration of treatment was of 18.3 ± 9.4 months. No patients had a history of eye surgery or laser. The average preoperative IOP was 28.3 ± 6.1 mm Hg and after the study the patients were followed for 15 months.

After all preoperative tests were performed and written informed consent was obtained, a laser-assisted deep sclerectomy was performed by the same surgeon (CV). All cases were done after the patients received local anesthesia and sedation induced by an anesthetist. Preoperative topical treatment consisted of one drop each of norfloxacin and diclofenac every 30 minutes for 2 hours. One drop of topical tetracaine was administered every 5 minutes 3 times before cleaning the conjunctival sac with 5% betadine. The procedure started by creating a fornix-based 6-mm conjunctival incision and dissecting conjunctiva and Tenon's capsule. Superficial cauterization of the bleeding points was carried out, followed by the application of mitomycin C (MMC) 0.02% for 2 minutes, placed between Tenon's capsule and the sclera. The MMC was then washed out thoroughly with balanced saline solution for 30 seconds. A 4 x 4 mm flap (two thirds the scleral thickness) was then created, 1 mm into clear cornea. The Er:YAG laser was applied (10 mJ/20 Hz) to the scleral bed under the flap over an area 3 x 3 mm and centred on Schlemm's canal. Laser ablation thins the scleral tissue to the point that aqueous humour percolates through the deep sclera (Figure 1B). At this point the fluid absorbs the laser, although in some cases descemet micro perforations was done. After confirming the filtration of the fluid, the integrity of

the anterior chamber, and the absence of bleeding, the scleral flap was sutured with two 10/0 nylon sutures, and the conjunctiva was closed with the 10/0 nylon to achieve complete closure and avoid postoperative leaks. Postoperatively, topical diclofenac and norfloxacine were administered every 12 hours for 4 days. Topical diclofenac was continued every 12 hours for 2 weeks.

The follow-up examinations were done at 1, 3, and 7 days postoperatively, 2, 3, and 4 weeks postoperatively, and then every 3 months up to 15 months. At the follow-up visits, the best-corrected visual acuity (BCVA) and the IOP were measured. The patients were examined for the presence of an inflammatory reaction, filtering bleb, and hyphema, and the anterior chamber and the fundus were examined. At the 2, 3, and 4-week follow-up visits, gonioscopy was performed (Figure 1 A-C). To evaluate the postoperatively surgical induced astigmatism, Alpins vector analysis (ASSORT ®) was used[30].

Comparing the average values, using the Student's t-test for independent or coupled data, carried out statistical analysis. For comparing percentages, Pearson's Chi square test was used to compare the percentages, and the survival estimation by the Kaplan Meier method.

Results

Of the 46 consecutive eyes initially enrolled in the study, four, all of which had POAG, were lost to follow-up. Figure 2 shows the IOP values. Laser-assisted deep sclerectomy achieved a 46% reduction in IOP at 15 months compared with the preoperative IOP ($P<0.0001$) The average preoperative IOP decrease from 28.3 ± 6.1 to 14.1 ± 3.5 mm Hg at 24 hours ($P<0.0001$) and was maintained until the third month when it increased to 16.3 ± 4.2 ($P<0.0005$), this value subsequently decreased to 15.8 ± 3.9 mm Hg at 6 months ($P<0.0001$), which was maintained until the final examination at 15 months (15.3 ±2.7 mm Hg, $P<0.0001$). There was no substantial scattering of the results; (standard deviation, approximately ± 3.4 mm Hg). There was no statistically significant difference based on sex (Table 2). Patients under 50 years had greater variability compared with patients older than 50 years, although the IOP levels were similar and not statistically different. There were no differences among the three types of glaucoma, but there were only three patients with pigmentary glaucoma and two with pseudoexfoliative glaucoma, and the preoperatively IOP in these two small groups was slightly lower than the group with POAG. There was a difference

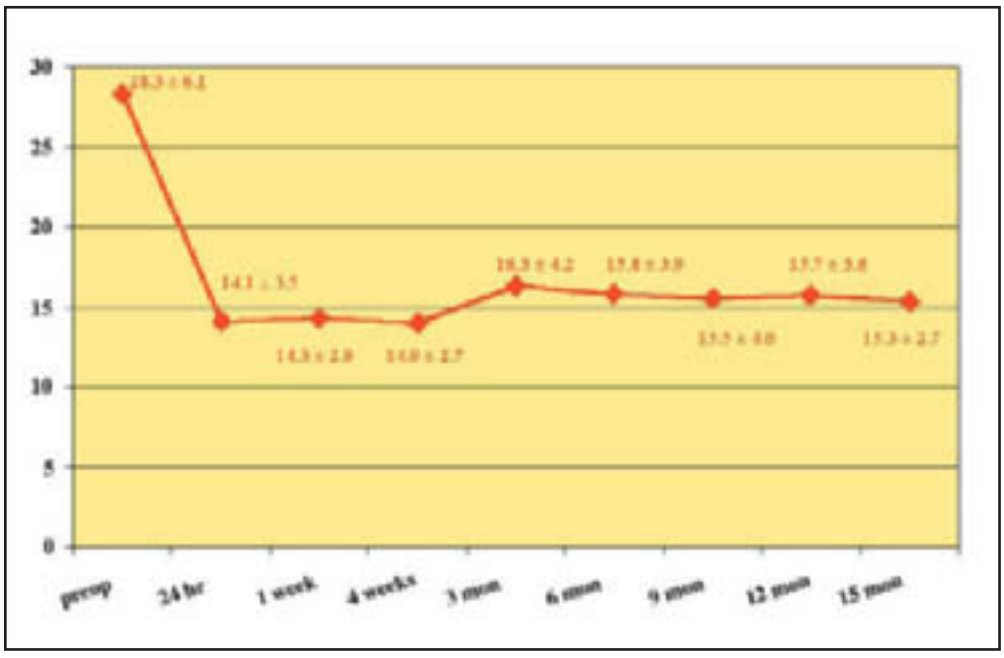


Figure 2. IOP values after 15 months of follow up.

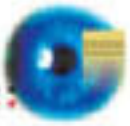


Table 2.
Preoperative and postoperative IOP after 15 month follow up.

	Preop IOP (mm Hg)	Postop IOP (15 mon.)
Female	27.3 ± 5.7	15.0 ± 2.5
Male	28.7 ± 6.2	15.5 ± 2.8
Age < 50 y	26.1 ± 5.8	15.1 ± 1.4
Age ≥ 50 y	29.3 ± 6.4	15.4 ± 1.0
POAG	28.5 ± 6.3	15.4 ± 1.0
Pigmentary glaucoma	26.2 ± 3.8	14.1 ± 0.9
Pseudoexfoliative glaucoma	26.9 ± 2.6	14.9 ± 1.1

Table 3.
IOP values.

	Preop IOP (mm Hg)	IOP post (15 mon)
Without previous glaucoma medication	26.8 ± 5.1	14.6 ± 1.9
With previous glaucoma medication	28.8 ± 6.3	15.5 ± 3.1
1 Medication	27.4 ± 6.8	15.1 ± 3.9
2 Medications	29.5 ± 5.1	15.8 ± 2.5
3 Medications	30.1 ± 4.3	17.9 ± 1.2
Evident filtering bleb	28.6 ± 5.9	14.5 ± 2.5
Flat filtering bleb	28.1 ± 6.5	15.9 ± 2.9
1 Week postop IOP < 15 mm Hg	28.5 ± 3.9	14.6 ± 2.1
1 Week postop IOP ≥ 15 mm Hg	28.2 ± 6..9	15.6 ± 3.0

between the patients with POAG who had not been treated previously and the patients who had been treated, but the difference did not reach statistical significance (Table 3). Compared with the patients who received topical medications, the patients who did not receive medication had lower postoperative IOP levels, more regular evolution of IOP postoperatively, and a smaller standard deviation. The difference became statistically significant when we analyzed the patients who received more than two medications and had a treatment period longer than 1 year, whether or not all three treatments had been used for that long ($P<0.006$).

In conventional trabeculectomy the absence of a filtering bleb is usually related to failure. In our case, the absence of the filtering bleb is not always related to the bad results, although, it is evident that its presence showed to be indicative of a longer period of IOP reduction. (Table 3). In the patients with a flat bleb, the results were more variable and the IOPs

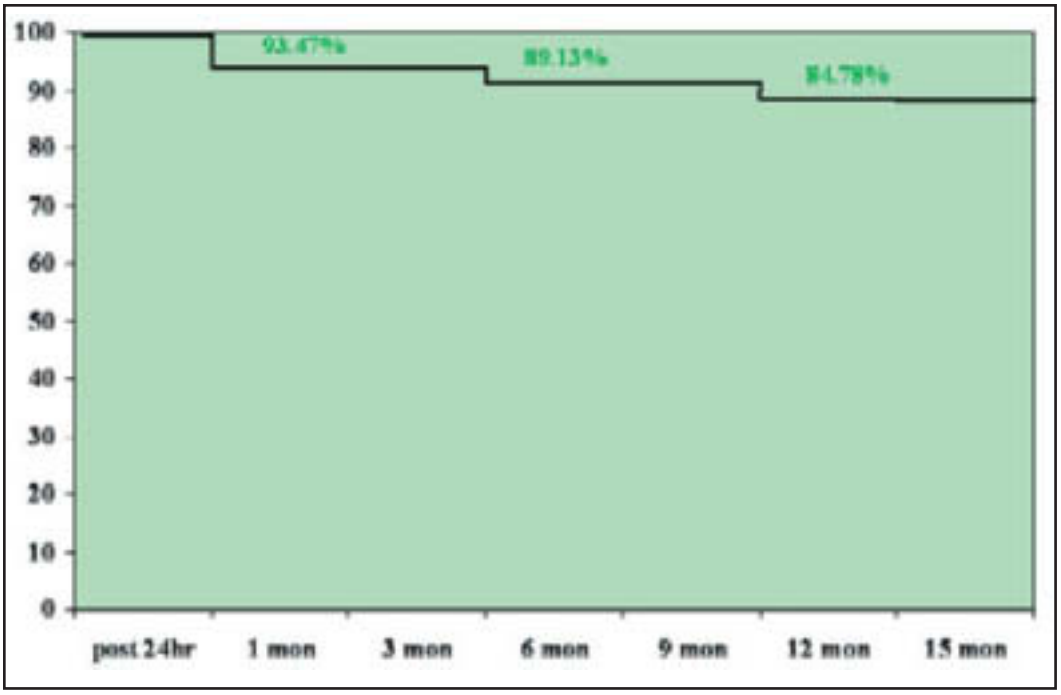


Figure 3. Cumulative complete success probability using Kaplan-Meier table analysis

tended to be higher. The eyes that maintained a filtering bleb had lower IOPs, less variability, and longer durations of lower IOPs levels (P<0.007).

The postoperative IOP level was more stable in eyes with a lower IOP during the first week after the procedure compared with those with a higher IOP. Those with an IOP under 15 mm Hg had a longer duration of decreased IOPs than the eyes with an IOP of 15 mm Hg or higher, although there was no statistically significant difference when all cases are considered together, but when analyzing the group of patients who had received 3 previous medical treatments, there was a significant difference (P<0.006) (Fig. 3). It is noteworthy that the eyes with the best results regarding IOP, variability, and maintenance of a decreased IOP level were those in which microperforations occurred in Descemet's membrane during sclerectomy with no substantial loss of aqueous humour, flattening of the anterior chamber, or peripheral anterior synechia seen in the postoperative period. In all cases there was an evident filtering bleb.

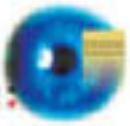


Table 4.
Surgical Failures.

Time of failure	Nº of eyes	Treatment	Result
1 Month	3	Subconjunctival 5FU + 1 medication	IOP controlled with 1 medication
6 Months	1	1 Medication	IOP controlled with 1 medication
	1	Trabeculectomy	IOP controlled without medication
12 Months	1	1 Medication	IOP controlled with 1 medication
	1	2 Medications	IOP controlled with 2 medications

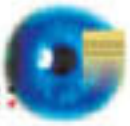
Failure was defined as an IOP higher than 18 mm Hg without topical treatment (Table 4); the first month three eyes had an IOP of 23, 22, and 26 mm Hg that were treated with subconjunctival 5 fluorouracil. All cases had an IOP lower than 18 mm Hg after treatment without topical medication. At the 6-month follow-up visit, two eyes had an IOP above the desired level. One patient had an IOP of 24 mm Hg (13 mm Hg during the immediate postoperative period) and a flat bleb. After a topical beta-blocker was administered, the IOP decreased to 17 mm Hg. In the second case, the IOP increased from 15 mm Hg immediately postoperatively to 26 mm Hg at 6 months with no bleb. This patient also was treated with a topical beta-blocker, and the IOP decreased to 19 mm Hg, which was not sufficiently low because there was clear visual field progression. A conventional trabeculectomy was performed, and the IOP decreased to 14 mm Hg without medical treatment. At 12 months, two additional eyes had IOPs of 23 and 22 mm Hg. Both were managed by adding topical dorzolamide. In one case, a beta-blocker also was added to the dorzolamide after 3 months. In both eyes IOP was reduced, 17 and 18 mm Hg respectively at the final control.

Table 5.
Complications in laser-assisted deep sclerectomy.

Complication	Nº	%
Hypotony (IOP < 5 mm Hg)	1	2.17
Choroidal detachment	1	2.17
Retinal detachment	0	0
Hyphema	3	6.52
Macular edema	1	2.17
Flat anterior chamber	0	0
Cataract	0	0
Visual acuity decrease	1	2.17
Perforation and conversion to trabeculectomy	2	4.35
Failure in IOP reduction (IOP < 21 mm Hg without treatment)	7	15.22

The surgical complications are summarized in Table 5. There was one case of hypotony (IOP lower than 5 mm Hg) with choroidal effusion. The patient was treated with a compression bandage and anti-inflammatory drug because there were no leaks or suture problems. The hypotony resolved in 3 weeks and normal visual acuity was recovered. Three cases of hyphema (6.5%) were resolved within the first few days postoperatively. It was done a scleral microperforation in one of the three cases. One case of cystoid macular edema was treated medically; the patient recovered partially and lost two lines of Snellen acuity at 15 months. There were no cases of flat chambers, retinal detachments, or cataracts. Two patients had perforations of Descemet's membrane during deep sclerectomy, and one procedure was converted to a conventional trabeculectomy. The other case did not require conversion to a full-thickness trabeculectomy because the perforation was discrete at the level of Descemet's membrane and the anterior chamber depth was not athalamic. There was a peripheral anterior synechia in the surgical area and the IOP on day 3 was 23 mm Hg (26 mm Hg preoperatively). A full-thickness trabeculectomy was performed on day 9. The IOP at 24 hours was 14 mm Hg, which was maintained thereafter.

Visual acuity analysis showed only one patient who developed cystoid macular edema and decreased visual acuity compared with the preoperative measurement. The rest of the eyes maintained



the visual acuity level, with small variations that did not reach statistical significance (0.83 ± 0.12 preoperatively, 0.80 ± 0.16 at 15 months). The visual acuity recovered at 1 and 3 days, with a reduction of less than one line of Snellen acuity. On day 7, all patients had recovered the preoperative visual acuity. Refractive error analysis showed a discrete change; the average induced astigmatism was –0.38 diopter at 173º according to vector analysis. As with the with-the-rule astigmatism, it did not seem to greatly affect the visual acuity.

Discussion

The results show that laser-assisted deep sclerectomy effectively reduces IOP, and the reduction is similar to that obtained using a conventional full-thickness procedure and a conventional non penetrating deep sclerectomy.[28] Published data show an average reduction in IOP of 53,2% when trabeculectomy is performed and 48.2% when deep sclerectomy is performed[31] Our series shows an average reduction of 46%, which is similar to the other reports. The present study shows how good results can be achieved using this technique, which is simple and reproducible. We used a laser that allowed ablation of the scleral tissue in a controlled manner; the laser was applied after a scleral flap was created to reduce scleral thickness to the point at which aqueous humour percolates through the deep sclera, and it is unnecessary to perform a careful dissection of Schlemm's canal and juxtacanalicular tissue, as in manual non-penetrating sclerectomy.

The area of ablation is 3 x 3 mm over Schlemm's canal and the laser is applied until the aqueous humor percolates, which means the sclera is sufficiently thin to ensure an effective reduction of IOP. This technique is simple for an anterior segment surgeon to perform; it has a short learning curve, which makes the procedure reproducible.

It is unclear how deep sclerectomy reduces IOP. We observed that the IOP levels remained low for a longer period in eyes in which there was an obvious filtering bleb, which possibly occurring with more aggressive laser-induced scleral thinning. In these cases microperforations in Descemet's membrane developed. There was no increase in the number of peripheral anterior synechia, and the IOPs were lower with no hypotony (IOP < 5 mm Hg). It seems that there is leakage of aqueous humor through the sclerectomy site into the sub-Tenon's-subconjunctival space, just as that occurring after a conventional full-thickness trabeculectomy, where good prognosis is indicated by the presence of a filtering conjuntival bleb. This goes along with the fact that the patients with increased IOPs had flat blebs. We do not think this technique is comparable to conventional trabeculectomy, but the two procedures have more similarities than other authors suggest [16,22,26] . We think that what makes this surgery different from the trabeculectomy proposed by Cairns is that the opening of the anterior chamber does not occur, although, in some cases microperforations are produced. We consider that the outflow occurs, basically, through the incision's borders of the scleral flap toward sub-tenon space. Percolation through the uveoscleral path is another alternative. In our technique the scleral thickness is reduced in a 3 x 3 area, and hypothetically, Schlemm's canal and the juxtacanalicular tissue are removed, which impose greater resistance on the outflow pathway. The inner trabeculum and Descemet's membrane remain, and the aqueous humour leaks through, although the aqueous then finds the scleral flap. We think that the aqueous humor leaks from the anterior chamber through the thinned sclera into the subscleral zone and then flows to the uvea and the subconjunctival space along the scleral incisions that remain partly open because of the effect of MMC.

The erbium:YAG laser simplifies the technique. There is no need for deep-plane scleral

dissection or identification of Schlemm's canal, its roof and floor, or the juxtacanalicular trabeculum. The dissection of all these structures is difficult and requires a learning curve, and some cases require converting to a full-thickness trabeculectomy because of inadvertent perforation.

We believe that it is important to review scleral implants as a method to reduce fibrosis. Our experience has not been fully satisfactory [29] . The work of Sourdille et al. showed that at 8 months postoperatively there was an intrascleral lake, which hypothetically explains the success of the procedure. We found that occluding the scleral flap, as they described, does not increase the success rate. There may be an alternative outflow pathway, such as an intrascleral lake that has been reported in other studies that does not always coexist with good IOP control.

In this study we showed that the highest survival rate and stability occur in eyes with an obvious filtering bleb, which may prove that the aqueous flows from the anterior chamber through Descemet's and the trabecular area toward the subconjunctival space, and encounters no resistance at the scleral flap incisions. The implantation of a device may keep these paths opened long term, but presently there is no device that guarantees this effect. Some of these implants are made of an absorbable material and may trigger a cicatricial reaction, others seem to favor blockage of the outflow path and fibrosis. We therefore decided to use antimitotic agents, which we disliked in principle, because they may facilitate complications, however, previous experience with these drugs enhancing conventional trabeculectomy allows their use in a reasonably safe manner. Until now we have not observed the development of serious complications caused by the antimitotic agents on deep sclerectomies, and their use has improved the survival of the procedure.

Despite complications, laser-assisted deep sclerectomy has advantages over traditional conventional trabeculectomy, and we think that the use of the erbium:YAG laser is a step forward, simplifying the technique and allowing most surgeons to perform it. The only drawback is the high cost of this technology.

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Chapter 27
TRABECULAR ASPIRATION AND GONIOCURETTAGE

Philipp Jacobi, M.D.

General Considerations

We have described two original techniques for the surgical management of primary open angle glaucoma, aimed at debridement of the trabecular meshwork. The effectiveness of these techniques is presently unknown. Conventional glaucoma filtering surgery is the mainstay for treating pathologically increased intraocular pressure. There is a growing trend toward performing surgery earlier in the course of glaucoma treatment. Despite an increase in success rates, however, filtering procedures are still plagued with several problems, such as hyphema, flattened anterior chambers, hypotony, and scarring. Especially in filtering procedures, tissue that is not primarily involved in the glaucoma process, like episclera or conjunctiva, is the main focus of treatment.

(An alternative to the standard filtering procedures is non-penetrating filtering surgery. In these procedures trabecular meshwork debridement is attempted through an external approach via the sclera. Another alternative is Dr. Jacobi's technique – **Editor**).

Based on the concept that pathological alterations of the trabecular meshwork and the endothelium of Schlemm's canal are responsible for IOP increase, trabecular surgery has to be regarded as specific glaucoma surgery. This surgery must be subject to scientific study. We have designed two different techniques for improving glaucoma surgery based on surgery to the trabecular meshwork and increasing aqueous facility of outflow via its physiological route instead of creating an external fistula.

Trabecular Aspiration

The first of these techniques is trabecular aspiration, which functions by the same principle as a vacuum cleaner. In certain sub-types of obstructive open-angle glaucoma, such as pigmentary or pseudoexfoliation glaucoma, in which the pathologically increased pressure results from obstruction of the intertrabecular spaces of the trabecular meshwork by debris such as pseudoexfoliative material or pigment granules, it would seem logical to clean the trabecular meshwork, leaving it free of debris. According to this principle, the trabecular aspirator, which in fact is an irrigation aspirator device, is applied to the trabecular meshwork. With instrument-tissue contact, suction pressure up to 200 mm/Hg is applied, and the meshwork is vacuum cleaned. In this way ocular facility can be increased, eventually resulting in pressure reduction.

We have been performing this procedure for more than 4 years. They first combined the procedure with cataract surgery since an experimental procedure cannot be conducted without another reason to enter the eye. Preliminary results showed a striking pressure reduction. In a Phase II study, conducted more than 3 years ago, Jacobi and colleagues began using trabecular aspiration as a primary, antiglaucoma procedure. The results have been promising.

Trabecular aspiration is familiar and an easy technique to master. All anterior segment surgeons do irrigation aspiration as part of phacoemulsification or extracapsular cataract extraction. Jacobi's technique involves nothing different but inserting the irrigation-aspiration probe in the proximity of the anterior chamber angle.

Trabecular aspiration differs from non-penetrating filtration surgery which is an elegant form of external filtration surgery, whereas trabecular aspiration involves an internal filtration in which the aqueous leaves the eye through Schlemm's canal.

(**Editor's Note:** The author does not explain why the trabecular meshwork, after being vacuumed cleaned does not become obstructed again by the same pigment or pseudo-exfoliative material which is still in the eye.)

Goniocurettage

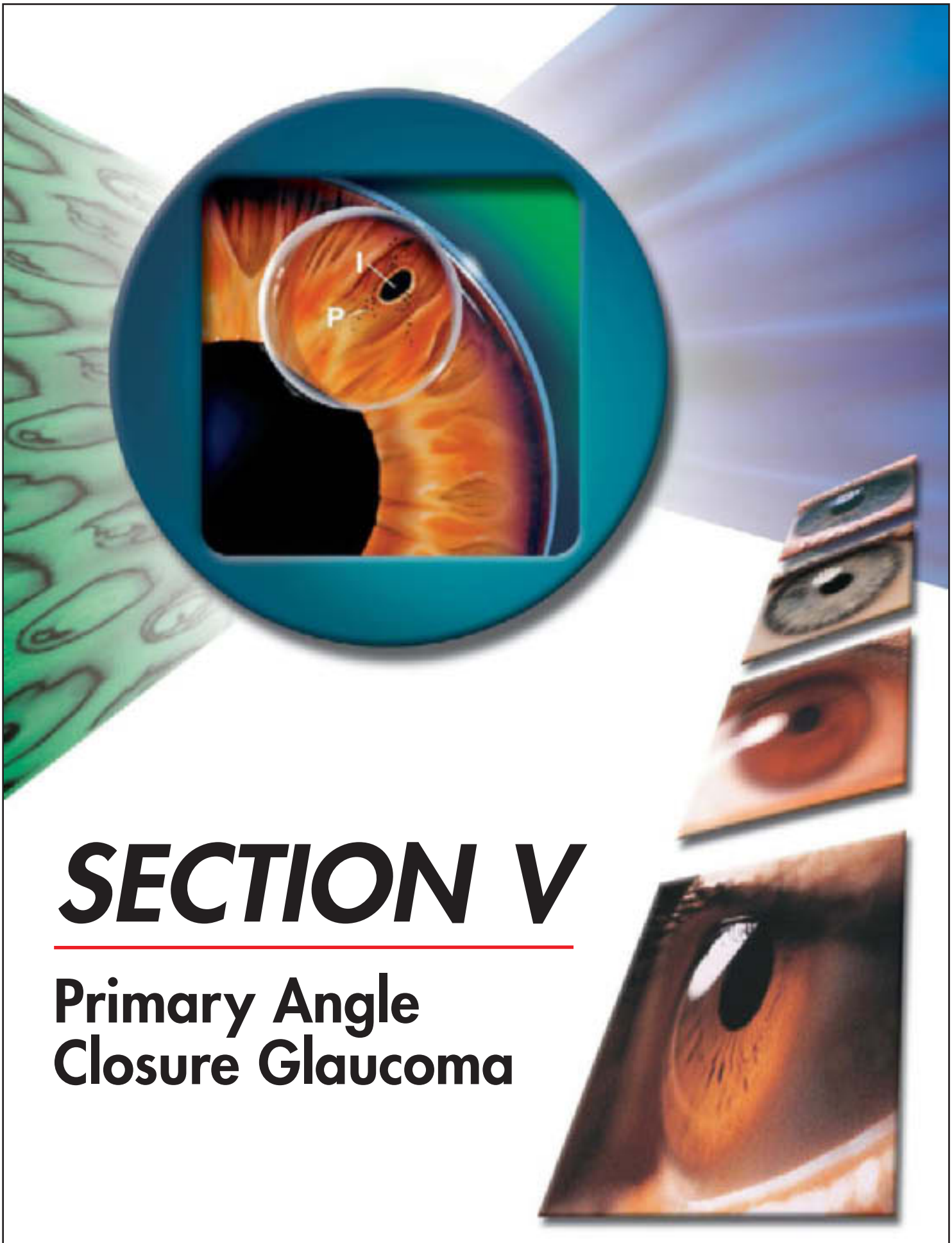
However, most sub-types of open-angle glaucoma are not caused by simple obstruction of the trabecular meshwork. Based on scanning and transmission electron microscopy in simple, primary open-angle glaucoma, outflow resistance can be caused by morphological changes within the trabecular meshwork. In these eyes aspiration would not increase ocular outflow facility. In these cases removal of the trabecular meshwork, would lead to some increase in ocular outflow facility. We applied the principle of goniocurettage in designing a new instrument like a small spoon or mini curette. Instead of incising the trabecular meshwork or performing trabeculotomy from the outside, he uses this curette to sweep through the trabecular meshwork removing some debris and opening the canal of Schlemm. For the past 1 or 2 years goniocurettage has been performed with a microendoscope inserted in the eye. We make two paracentesis, one for the surgical probe or curette, and one for the endoscope. The chamber angle surgery can be endoscopically controlled, especially in those cases where corneal opacification hampers visualization of the anterior chamber angle.

Results of Innovative Trabecular Surgery

Preliminary results from trabecular aspiration were so encouraging that we are now using trabecular aspiration as a routine procedure in pseudo exfoliative eyes with good prognosis.

Goniocurettage has now been applied successfully to quite a few patients with intractable open-angle glaucoma that has failed to respond to previous filtering procedures.

The main advantage is that the profile of the side effects, if not virtually zero, is very minimal. Shallow anterior chambers or hypotony never result. The major drawback is that pressure reduction is not as low as it is in filtering surgery because natural resistance to outflow within the trabecular meshwork remains. Future studies are needed to decide whether pressure reduction achieved by trabecular aspiration in the individual patient is low enough to prevent increasing damage to the optic nerve. About 70% of our patients who have been treated with trabecular aspiration have satisfactory pressure reduction. Thirty percent require adjunctive medication or additional surgery like a filtering procedure.



SECTION V

Primary Angle Closure Glaucoma

Chapter 28
ACUTE AND CHRONIC ANGLE CLOSURE

Benjamin F. Boyd, M.D., F.A.C.S.
Maurice Luntz, M.D., F.A.C.S.

Selecting the Operation of Choice

In this disease, it is particularly important to select the operative procedure most likely to initially succeed, in order to spare the patient a second surgical procedure. Surgery (laser or invasive operations) is always the treatment of choice since these patients cannot be cured with medical therapy.

Most cases do well with peripheral iridectomy, which is the operation of choice. This procedure can be done preferably with the Nd:YAG Laser[1] (Figs. 4 and 5). If the Nd:YAG laser is not available, Argon Laser Iridectomy is the second choice.[2, 3] If none of these lasers are available or adequately working at the time, the green diode laser can be used or incisional peripheral iridectomy is an excellent operation. However, if following attempted reversal of the acute episode with medical therapy, the angle remains more than 75% closed even with indentation gonioscopy and/or if the intraocular pressure remains over 45 mm Hg on full medication, the prognosis for peripheral iridectomy is very poor (success rate of only 43% as demonstrated by **Luntz**). In these cases or when the acute attack has lasted more than seven days, a filtering operation is the procedure of choice, mainly a trabeculectomy with mitomycin.[4]

Luntz has emphasized that in these bad cases a standard trabeculectomy is successful in controlling intraocular pressure in only 60-65% of eyes. When combined with mitomycin the success rate is 85% or better. The added postoperative risks of these procedures are acceptable because of the significantly higher success rate.

Arthur Lim has observed in Singapore that argon laser pupilloplasty or iridoplasty is a very effective method of treating acute angle closure glaucoma instead of surgery[5] (Fig. 6).

Emergency Medical Treatment

Immediately following the diagnosis of an acute episode of angle closure glaucoma, emergency medical therapy should be administered in an attempt to lower the pressure until the iridectomy (surgical or laser) can be done. Laser Iridectomy should not be performed in congested or inflamed eyes. Clear media are essential.

Dorzolamide administered topically is quite useful in reducing the severely elevated intraocular pressure and helping to successfully manage the acute episode. A beta-blocker may also be instilled. One vial of Acetazolamide may be administered intravenously very slowly and glycerin given by mouth, one gram/kilo of weight. The latter may produce nausea and vomiting. Instead of giving glycerin to the patient, Mannitol 20% solution administered IV, one gram/kilo of weight, 100 gtts/minute is the most effective drug to lower the intraocular pressure. If the patient has diabetes or cardiac problems, it should be administered slowly.

There is no response to miotics when the intraocular pressure is above 40 mm Hg. Once the pressure is below 40 mm Hg, pilocarpine is administered topically every hour until miosis is obtained.

ARGON LASER IRIDECTOMY (IRIDOTOMY)

Because of the coagulating effect of argon laser light, iridectomy performed by argon laser offers advantages over incisional iridectomy or neodymium: YAG laser iridectomy in patients predisposed to bleeding conditions, such as those taking anticoagulants or with known blood-clotting disorders. The laser iridectomy is performed as an office procedure in a closed eye —a considerable advantage over surgical iridectomy. It is an effective way of producing an opening in the iris but should **not be used in congested or inflamed eyes**. Clear media are essential. The eye is prepared with topical anesthesia. The surgeon should have comfortable arm supports.

In Figs. 1,2 and 3 we are showing Abraham's original technique advocating preliminary stretch burns to facilitate the iridectomy.(6) This technique is highly useful and effective. These burns immediately cause iris contraction and put the iris crypt on stretch. Other surgeons find that the stretch burn is generally unnecessary if the Abraham contact lens is used. (**Editor's Note**: Nd:YAG laser is the laser of choise for laser peripheral iridectomy).

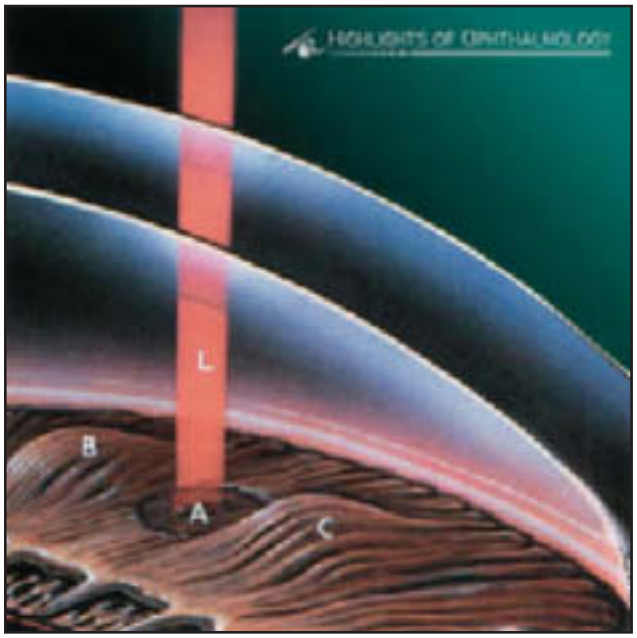


Fig. 1: Abraham's Argon Laser Iridectomy Two-Step Technique - Cross Section View of First Burn

This cross section view of the anterior chamber shows the configuration of the iris during the primary burn. Laser beam (L). Partially penetrating burn (A). Resulting iris humps (B) and (C). This completes the first burn.

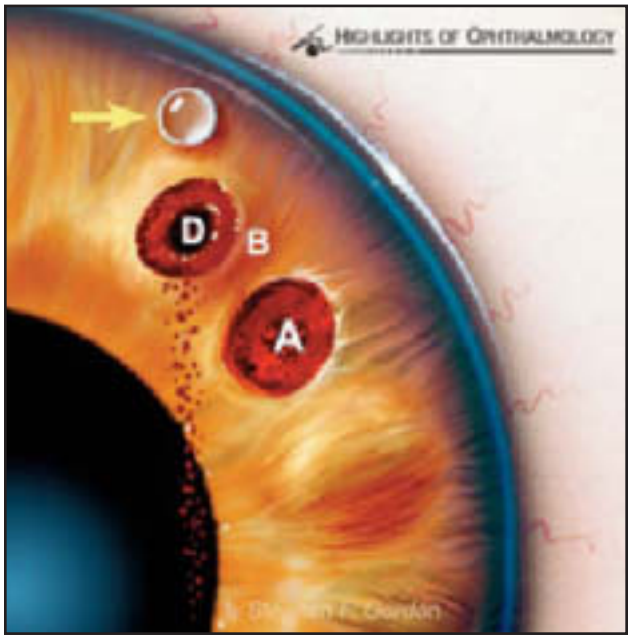


Fig. 2: Abraham's Argon Laser Iridectomy Two-Step Technique - Surgeon's View of Second Burn

The second burn is a penetrating burn aimed at the crest or peak of one of the iris humps (B) which resulted from the first burn. This second burn has now created a hole or iridectomy (D) through the peak of the iris hump (B). The first burn, which was partially penetrating, is shown in (A). Note iris pigment drifting down while gas bubble floats superiorly (arrow). Use the plano-convex button of the lens only for coagulation No. 2.



Fig. 3: Abraham's Argon Laser Iridectomy Two-Step Technique - Cross Section View of Second Burn

This cross section view shows the second burn in progress. The surgical view is shown in Fig. 2. Tangential laser light (L) hits and penetrates the peak of the iris hump (B). The primary burn is shown at (A). The laser light (L) is directed tangentially to prevent the light from striking the posterior retina. Even though the beam is tangential to the hump, it still strikes the Abraham lens in a perpendicular fashion to prevent reflection of the beam and resultant loss of power.

Argon Laser Iridectomy Technique

We are describing two important Argon Laser Iridectomy Techniques: 1) the **Abraham** technique[6] ; 2) the Luntz technique which we are describing in the text, which is as follows: A drop of apraclonidine 1% is instilled in the eye to be operated on 30 minutes before the procedure. Dorzolamide may be used if Apraclonidine not available. The patient is seated at the slit lamp, which is connected to the laser and is the outlet for the laser beam. A drop of topical anesthesia is instilled in the eye to be operated on, and the patient's head is placed in the slit lamp headpiece, ensuring that he/she is comfortable. An Abraham lens (plano lens with a +66 D button eccentrically placed) is applied to the cornea after filling the cup with gonioscopic fluid. The Abraham lens serves to concentrate the laser energy on the iris and defocuses the beam as it passes through the cornea, minimizing corneal epithelial burns. The +66 D lens also magnifies the area of iris selected for iridectomy. The presence of the lens stabilizes the eye, ensures adequate exposure of the peripheral iris and prevents blinking.

The slit lamp and laser are activated and the parameters set. The procedure is performed under high power (x16). An optimal site is between 10 and 2 o'clock, the upper nasal quadrant the most widely used. The site of the burn should be at the junction of the middle and outer third of the distance from the pupillary margin to the iris root. When completed, the iridectomy should be covered by the upper lid; otherwise, the patient may experience diplopia or other optical effects. Generally, an iris crypt or other site of thin stroma is selected. In a blue or lightly pigmented iris, a suitably located iris freckle is sought.

Luntz commences with a single contraction burn, using a 250-micron aperture, with 1.5W power, 0.1 sec. duration. The spot size is then reduced to 50 microns, using 1.5W, 0.1 sec. **An opening is burnt through the iris in the center of the original burn**. This is achieved by using a rapid sequence of burns until iris penetration is achieved. As soon as penetration is achieved, the laser power should be reduced to 0.75W or 1W. During the procedure, the previously chosen crypt is found and brought into meticulous focus. The patient must not be looking directly towards the laser. The gaze can either be slightly up or in, or both, in order to ensure that the laser will not cause a burn on the posterior pole of the retina.

Luntz emphasizes that the application of burns should be stopped if: 1) the iris surface chars (i.e., turns black), with no visible iris penetration. Under these circumstances, another site in the iris should be sought. If the same phenomenon occurs, the iridectomy should be abandoned in favor of a Neodymium YAG laser iridectomy. 2) the corneal epithelium shows multiple milky spots of the cornea, indicating that corneal burns are occurring. 3) opacities of the endothelium occur indicating endothelial burns. 4) the anterior chamber becomes turbid from pigment dispersion. 5) 150 burns have been applied at one session.

In all of the above circumstances, a second session is necessary. In the majority of cases, an iridectomy is achieved at the first session.

As penetration of the iris stroma reaches the pigmented epithelium of the iris, bursts of pigment appear in the anterior chamber ("smoke signals"). Power is then reduced to 0.75W, and further burns applied until a mushroom cloud of aqueous and pigment balloons through the iridectomy, indicating penetration of the iris. The anterior chamber will usually deepen at this point. The iridectomy is then enlarged by continuing to burn at the margins of the iris opening ("chipping away"), thus increasing the iris opening to about 100 microns. Loose pigment within the iridectomy or residual strands of iris stroma should be eliminated.

Criteria for Success

Patency of the iridectomy must be checked at the end of the procedure by noting a red reflex on retroillumination, or by visualizing lens capsule on direct slit lamp examination.

Gonioscopic confirmation that the angle has widened does not indicate a full thickness perforation. The angle widens if one simply breaks up the pathophysiologic "adherence" between the sphincter and lens. This often is a result of contracture of the coagulated radial fibers, while performing step 1, the partially penetrating burn.

Post-Operative Management

Post-operatively, apraclonidine 1% is instilled at the end of the procedure. Its use pre and postop is an important advance to prevent the frequently associated intraocular pressure spikes following laser iridectomy (as well as laser trabeculoplasty and posterior capsulotomy). A drop of topical prednisolone acetate 1% should be instilled and, two hours post-operatively, IOP is checked to ensure that it has not increased as a result of the surgery. If IOP is elevated, medication should be given to reduce it before discharging the patient. The patient is then requested to use prednisolone acetate 1% q.i.d. for 5 days in order to prevent iritis and inflammation.

Brown and Light Blue Eyes

In patients with extremely dark brown eyes and in those with very light blue eyes, it is difficult to achieve patent iridectomies using the argon laser. On the other hand, when performing Nd:YAG iridectomy, iris pigmentation is not relevant and the YAG instrument is the instrument of choice in very lightly pigmented irides.

ND: YAG LASER IRIDECTOMY

Nd:YAG laser iridectomy is presently the procedure of choice for all laser iridectomies. The **YAG** laser has proven to be a better tool for creating an iridectomy more quickly and more effectively. The holes obtained with the YAG laser tend to close less often. The YAG is also effective in light-blue irides and in very thick, heavily pigmented, brown irides as well, in which it is very difficult to achieve a permanent iridectomy with an argon laser. Proliferation of pigment or fibrous material does not occur with the YAG laser iridectomy so that a lasting, clean hole is commonly produced.

Energy Level

As with an argon laser iridectomy, we must use a lens, such as the Abraham or Wise, to condense the YAG laser energy. The amount of energy used depends on the iris thickness and pigmentation e.g. 5 shots, ranging from 5.5 to 6.5 millijoules: 5.5 millijoules for the ordinary iris and 6.5 millijoules for an iris that appears thicker and shows extremely heavy pigment by slit-lamp examination.

YAG Laser Iridectomy Technique

The patient should be on weak-strength miotics prior to therapy. These should be instilled 30 minutes prior to the procedure, in order to insure that the iris is taut and the pupil miotic. The technique advised by **Luntz** is as follows: The pre-operative preparation of the patient is similar to that described for argon laser iridectomy. The YAG laser may be used in the Q-switched short pulse mode (Frankhauser) or mode-locked form (Aron-Rosa). The infrared beam acts as a photodisruptor and is effective with extremely high energy and very short pulse durations.

Iris pigmentation is not relevant, and the YAG laser is the instrument of choice for very lightly pigmented irides. Careful focusing of the laser beam to the surface of the iris stroma is essential. The site selected for the iridectomy is more peripheral than with the argon laser in order to minimize the risk of lens damage. The procedure is facilitated if it can be done within an iris crypt (Fig. 4). An Abraham lens is used, and the laser iridectomy is performed superiorly (Fig. 4).

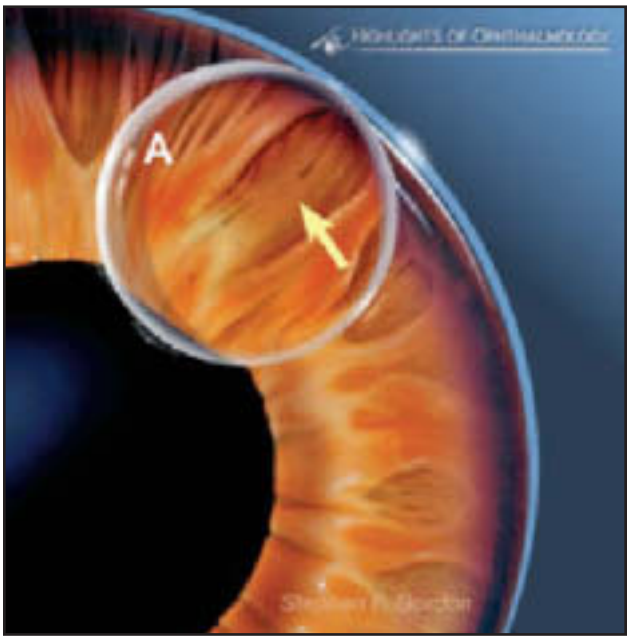


Fig. 4: Nd:YAG Laser Iridectomy - Luntz' Technique (Stage 1)

The +66D Abraham lens (A) magnifies a selected area of the peripheral iris within a crypt or thin stroma between 10 and 2 o'clock (arrow). The YAG laser may be used in the Q-switched short pulse mode (Frankhauser) or mode locked form (Aron-Rosa).

The YAG laser is programmed at 8mj, using initially two pulses per burst in a phakic patient and five pulses per burst in an aphakic or pseudophakic patient. The beam is carefully focused on the iris the laser is activated, and the first two pulses delivered. The aperture of the YAG laser beam is preset at 50 microns — the surgeon does not have the ability to change this. If there is no pigment dispersion at the end of the bursts, or if the stroma is obviously not being penetrated, a second burst is given. No more than two bursts should be delivered at each site. If penetration of the iris does not occur after two bursts, another site is selected and the same procedure followed. Lens capsule is not always seen at the endpoint, and transillumination is not always detected. The endpoint is usually recognized by the escape of iris pigment into the anterior chamber and deepening of the chamber as the iris is penetrated (Fig. 5).

A small iris hemorrhage may occur at the time of the laser burn; this is easily stopped by pressing on the eye with the goniolens for a few seconds. If the iris is vascularized, pre-treatment at the site of the iridectomy with the argon laser will prevent bleeding during the procedure. The short time needed for delivery of the energy with the YAG laser is an advantage in patients who are unable to keep still enough for argon laser treatment. The pre and post-operative care are similar to that described for argon laser iridectomy.

Differences Between the Argon and YAG Laser Iridectomy

The main differences as clarified by **Luntz** are: 1) The argon laser creates a burn through its thermal action and is dependent on pigment to produce this thermal action. The YAG laser produces an iridectomy through photodisruption of tissue and is independent of the amount of iris pigment present. 2) The argon laser delivers less energy with a longer pulse duration than the YAG laser to achieve iridectomy. 3) The site selected for the YAG laser is more peripheral than with the argon laser. 4) The aperture

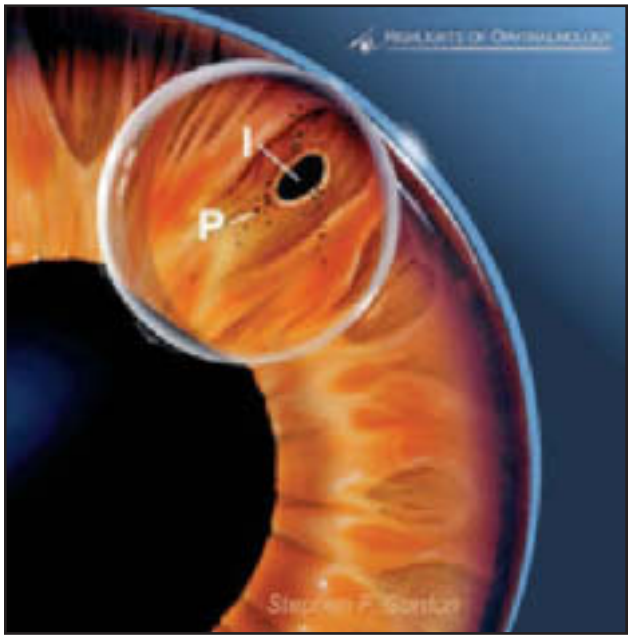
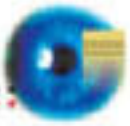


Fig. 5: Nd:YAG Laser Iridectomy - Luntz' Technique (Stage 2)

The infrared beam is carefully focused to the iris stroma and activated. Penetration of the iris stroma is usually noted by the escape of iris pigment (P) into the anterior chamber and deepening of the chamber. The resulting iridectomy is shown (I). No more than two bursts should be delivered at each site.



of the YAG laser is +50 microns and is fixed. 5) Once an opening is achieved with the YAG laser, it should not be enlarged with the YAG laser, as there is a risk of rupturing the anterior lens capsule with YAG laser energy. However, the argon laser can be tried at this stage to enlarge the YAG laser opening as the argon laser energy does not rupture the lens capsule. 6) The openings made by the argon laser may close post-operatively as a result of proliferation of pigment. This occurs in about 10% of eyes. It is extremely rare for YAG laser openings to close. 7) The YAG laser iridectomy has the potential of causing rupture of the lens capsule, and this has been documented in rare cases. There has been no documentation of lens capsule rupture with the argon laser. 8) The YAG laser delivers its energy over a very short time period to produce an iridectomy compared to the argon laser.

Felix Sabates[7] considers that YAG laser iridectomy has the following additional advantages over argon laser iridectomy besides those outlined by **Luntz**: 1) It uses several hundred times less energy to produce the desired effect than with the usual photothermal technique (argon blue-green or green). 2) Since the infrared energy is delivered at a high angle (16º) it is less likely to damage the retina. 3) It is most successful in cases of acute glaucoma where in spite of vigorous systemic and topical medication the intraocular pressure remains above normal. In these patients, usually the iris is very edematous and photothermal iridectomy is often unsuccessful or requires very high levels of energy. In the majority of these patients peripheral iridectomy can be accomplished successfully with neodymium YAG laser utilizing less energy.

Postoperative Management

It is important that topical corticosteroids and glaucoma therapy be continued until the inflammation has stopped and the iridectomy is patent. The intraocular pressure should be carefully observed and monitored. If a pressure spike occurs, this can be managed promptly with adequate medications. After it is clear that the iridectomy is open, pilocarpine should be stopped whenever possible. The pupil should be periodically dilated during the first month to prevent posterior synechiae.

Following laser iridectomy, the patient continues using miotics for at least 3 weeks until permanent patency of the iridectomy is established. Topical steroid drops may be given on the same day and will usually suffice to control postoperative inflammation (prednisolone acetate 1.0% every 2 hours). A cycloplegic is rarely necessary since the iritis is mild and transient and has usually totally resolved by the following morning.

Management of the Second (Fellow) Eye in a Patient with Primary Angle Closure

Luntz has emphasized that the fellow (second) eye in a patient who has suffered a typical acute attack of unilateral primary angle closure glaucoma will have an anterior chamber of approximately equal narrowness to the involved eye and is exposed to a high risk of an acute angle closure attack. It has become routine to perform a prophylactic peripheral laser iridectomy in fellow (second) eyes of patients with unilateral primary angle closure glaucoma.[4]

Patients with anatomically narrow angles who are asymptomatic should have prophylactic laser iridectomy in both eyes if the angles are Grade 1 open or narrower.

If neither argon or YAG laser are available, the surgeon may perform prophylactic "invasive" or incisional surgery in the fellow (second) eye only in those patients who have a definite previous history or symptoms of acute episodes of angle closure, or the angle is slit open.

When these above criteria are absent, invasive surgery is not usually performed in the fellow (second) eye, but careful re-evaluation of the history and gonioscopy is repeated approximately every 4 months. The patient must be made familiar with the symptoms of an angle closure episode and must be told to report immediately if any of these symptoms occur.

(**Editor's Note**: **Arthur Lim, M.D.**, one of Asia's most prominent ophthalmic surgeons and teachers, has emphasized for years that primary angle closure glaucoma is more prevalent in Asia than it is in the West and that more than half of glaucoma in Asia is of the primary angle closure category. **Lim** considers that this disease is one of the most important blinding conditions in the world in part because of an aging population.)

CHRONIC ANGLE CLOSURE GLAUCOMA

Chronic angle-closure glaucoma refers to an eye in which **portions** of the anterior chamber angle are permanently closed by peripheral anterior synechiae. The clinical history is varied. Chronic angle closure glaucoma (ACG) may be primary or secondary. In primary, primary angle closure glaucoma (ACG) usually occurs following an acute attack treated by peripheral iridectomy in which mild acute attacks continue resulting in angle closure by peripheral anterior synechiae (PAS). Secondary ACG occurs for example, after intraocular surgery complicated by wound leak and delayed reformation of the anterior chamber. This type of glaucoma is very common among black patients. The trabecular meshwork in these eyes is markedly impaired.

This is in contrast with primary angle closure glaucoma which is less common among blacks. Synechial angle closure can occur without or preceeding acute angle closure and these cases of chronic angle-closure glaucoma usually do not have a history of ocular pain, congestion, or corneal edema as is the case with acute angle closure. Intraocular pressure may be normal or elevated and glaucomatous damage may or may not be present.

The synechial closure usually begins superiorly where the angle is narrowest and progresses inferiorly. The peripheral anterior synechiae are broad or tent-shaded and are attached to the top of the scleral spur or the posterior trabecular meshwork. They are not as anterior as those seen in acute-angle closure.

Eyes with chronic closed angle glaucoma in which more than 75% of the angle is closed or with secondary angle closure glaucoma, in whom the intraocular pressure cannot be reduced below 35mm Hg with medication are eyes with inadequate trabecular function. Eyes in this category need a trabeculectomy with mitomycin as the first treatment choice.

Iridoplasty (Gonioplasty) - Opening a Narrow Angle With the Laser

In patients with chronic narrow angle glaucomas, an attempt can be made to open these angle with the argon laser by means of Iridoplasty (Fig. 6). This procedure consists of applying the argon laser to the mid-stroma. The laser produce heat in the iris, which causes collagen shrinkage.

In the case of acute or chronic angle closure, a peripheral iridectomy with the laser is the procedure of choice if the angle can open in over 50% of its surface. However, occasionally the peripheral iris will be so close to the cornea that you cannot safely use the laser nor make a peripheral iridectomy where you would want it to be. In those cases, it is sometimes beneficial to apply laser spots to the mid- or central portion of the iris, which will produce iris shrinkage and will often open the angle (Fig. 6). This procedure is known as **Laser Iridoplasty (Gonioplasty)**. Some surgeons use this procedure for the treatment of acute angle closure glaucoma in place of laser peripheral iridectomy.

Another indication for this procedure would be at the time of laser trabeculoplasty, if you have difficulty in viewing the angle because of an iris plateau (Fig. 6).

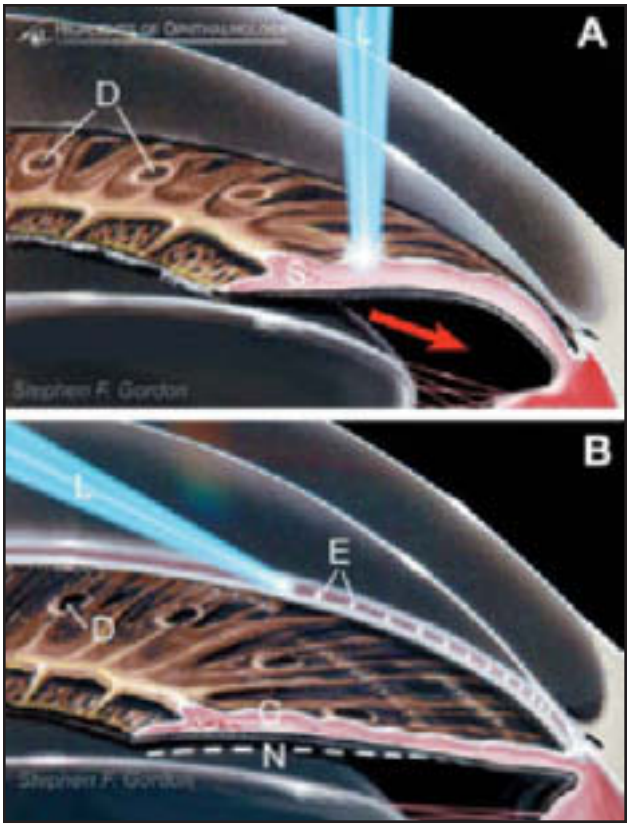


Fig. 6: Iridoplasty with Argon Laser - Opening a Narrow Angle in Chronic, Narrow Angle Glaucoma

A laser iridectomy is the procedure of choice for narrow angle glaucoma, except in cases such as **(A)** above where the peripheral iris lies too close to the cornea for treatment. Laser applications (D) are placed in the mid-stroma area of the iris to open the angle. These non-perforative laser applications cause heat which in turn causes shrinkage of the iris collagen fibers in the direction of the arrow. The iris sphincter muscle (S) and laser beam (L) are shown. In **(B)**, shrinkage from laser applications (D) has opened the angle to an acceptable position (C). A peripheral laser iridectomy is then executed. The normal iris location is shown on dotted line (N). The angle is now sufficiently open for laser trabeculoplasty if indicated. Laser beam (L) is shown producing burns (E) in the now visible trabeculum.

The procedure of choice requires application of laser burns of a large spot size (100-200 microns) and a **very low power** setting for a short duration of time. We do not want to produce large burns, but just enough elevation in temperature to create collagen shrinkage.

By causing shrinkage in the mid-zone of the iris (meaning the area between the sphincter and periphery), you shorten the distance between the pupil and the periphery, thereby pulling the iris away from the peripheral angle. This is carried out by using approximately 4 to 5 large spot-sized laser burns in each quadrant, and placing them essentially equidistant, 360º around the surface of the iris.

Technique for Gonioplasty (Iridoplasty)

Apraclonidine eyedrops are used prophylactically, and the eye is anesthetized with topical anesthesia as described for ALT. The patient is placed at the slit lamp, and a two- or three-mirror Goldmann goniolens is inserted in the eye as described for ALT. The laser is set at an aperture of 200 microns, 0.1 sec. duration and 1.5W power. The periphery of the iris is visualized through the goniolens, directing the laser beam to the height of the convexity of the iris (the iris will be "bombe", producing a narrow angle, the height of the convexity of the bombe iris is the

area treated). Once the laser beam is placed in the right position, again over the inferior half of the angle, the first laser burn is placed at the nasal or temporal edge of a 180º -span of the inferior angle. The laser is activated, and a burn is produced on the iris, causing contraction of the iris. If an iris retraction is not achieved, power can be increased until a burn occurs and the iris retracts. This is repeated across the 180º of the inferior angle, generally using 12-15 burns. This procedure will cause retraction of the iris, in this way, opening the angle, so that it can be adequately visualized for ALT.

In eyes that we are contemplating a laser trabeculoplasty (ALT), we must be sure we are not dealing with a shallow angle with plateau iris (Fig. 6). Plateau iris is caused by abnormally positioned ciliary processes. If one performs a laser trabeculoplasty in a shallow angle, with the root of the iris in close proximity to the angle, one can zipper up the angle with peripheral anterior synechiae . Therefore, if the angle is shallow, one should do laser iridectomy first and do a laser trabeculoplasty (ALT), if indicated, a few weeks later. Another alternative is to perform a laser iridoplasty (Fig. 6), followed by trabeculoplasty.

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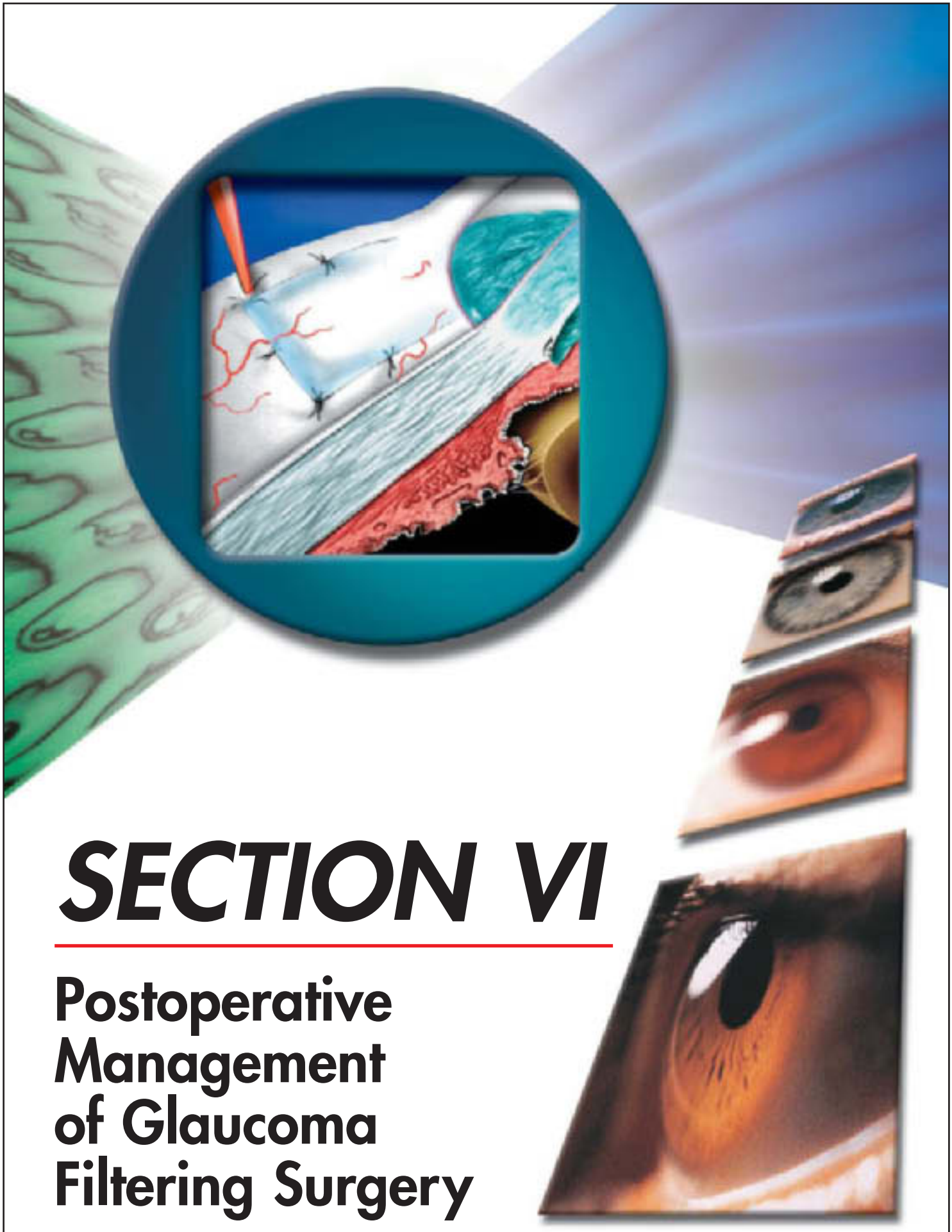
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SECTION VI

Postoperative Management of Glaucoma Filtering Surgery

Chapter 29
ENHANCING THE RATE OF SUCCESSFUL FILTRATION

Benjamin F. Boyd, M.D., F.A.C.S.
Maurice Luntz, M.D., F.A.C.S.

Important Precautions and Intraoperative Measures

Richard Parrish recommends the following measures: 1) For patients with **neovascular glaucoma**, we can increase the likelihood of success by addressing first the primary ischemic problem in the retina. In proliferative diabetic retinopathy a panretinal photocoagulation should be performed **before filtration surgery** is considered.[1,2] **Parrish** makes clear that cases of neovascular glaucoma require prior treatment of the primary, posterior-segment disease **before filtration** to diminish the stimulus for new vessel growth.

2) Meticulous attention to **hemostasis** is very important **during filtering surgery** because blood contains growth factors that enhance the proliferation of fibroblasts in the subconjunctival space. **Parrish** tries to achieve hemostasis with minimal tissue necrosis since such necrosis produces more inflammation and increases the likelihood of scarring.

3) A third important point is to **correctly select the site for filtration** by selecting conjunctiva that is freely movable, although not necessarily conjunctiva that has not been operated previously. If the conjunctiva is movable at the superior limbus after cataract surgery, it is easier to operate at a superior position than inferiorly. To test for scarring of the conjunctiva, **Parrish** injects sterile balanced saline solution (BSS) through a 27-gauge needle, approximately 8 mm posterior to the limbus. If the conjunctiva elevates easily up to the anterior limbus under the force of the BSS, a technically uncomplicated filtering surgery with a limbal based flap or a fornix based flap is possible. If, however, the conjunctiva is recessed and scarred to the episcleral surface, as so often happens after cataract surgery, the chances of achieving filtration are much less. At that point, we can go to an infranasal or infratemporal quadrant. If we are operating below in the infratemporal or infranasal quadrants, exposure is the primary problem. We may use a corneal-traction suture to elevate and adduct the eye and sit on the same side of the patient as the eye that is being operated. In this manner, the filtering site is directly in front of us. (The inferior conjunctiva is thinner than superiorly and has less eyelid protection. Many surgeons prefer to avoid this area as there may be a higher incidence of endophthalmitis - Editor).

4) Minimizing wound leaks is fundamental. Perhaps one of the most important intraoperative variables is an absolutely water tight conjunctival closure, **particularly when using the antimetabolites, 5-fluorouracil (5-FU) or mitomycin**, which we will discuss later in more detail. Conjunctival wound healing at the filtering site is retarded with 5-FU and mitomycin, and wound leaks may occur along the needle tracts as well as along the suture line. When using a **vascular-taper needle** wound leakage is minimized. The worst needle for this par-

ticular suturing is the spatula type, because it cuts a slit in the conjunctiva that is not completely filled with the suture. (This point is controversial and many surgeons successfully use a spatula type needle with 10-0 nylon - **Editor**). When operating down below, leakage can occur even when 5-fluorouracil is not used. To test the water tightness of the closure, **Parrish** fills the anterior chamber with saline through a previously made paracentesis tract and looks for leaks after suturing the conjunctiva together.

Main Goals in Postoperative Management

The goal of postoperative management is to ensure adequate long-term filtration. **Maurice Luntz** considers that the following principles are important: 1) minimize postoperative inflammation;[3,4] 2) avoid postoperative hypotony[5]/ocular hypertension; 3) enhance bleb formation; 4) avoid late infection of the bleb. These goals can be achieved by meticulous surgical technique, frequent and careful postoperative evaluation of the operated eye, and early detection and aggressive treatment of complications.

Minimize Postoperative Inflammation

Luntz emphasizes the following measures: 1) careful, minimally traumatic surgical technique (e.g., a fornix-based conjunctival flap requires less dissection than a limbus-based flap); 2) the use of post-operative topical antibiotic/steroid combinations and, if necessary, subconjunctival (or sub -Tenon's) steroids and/or systemic steroids;[6] 3) Topical cycloplegics; 4) in severe post-operative inflammation unresponsive to steroids, cytotoxic agents (e.g., cyclosporine - A). The use of intraoperative mitomycin - C or 5-FU is also helpful to reduce post-operative inflammation.[4]

Avoid Postoperative Hypotony

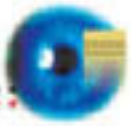
Hypotony related to hyposecretion or hyperfiltration and consequent shallowing of the anterior chamber can result in a variety of undesirable events, such as flattening of the bleb, corneal or lenticular decompensation, cystoid macular edema or papilledema. **Luntz** recommends the following precautions and **aggressive treatment** for post-operative hypotony:

a) Adequate suturing of the scleral flap during a trabeculectomy procedure to prevent excessive leakage through the cut ends of the flap in the early post-operative stage. If a tube shunt implant is used, the tube can be tied during surgery or a suture placed within its lumen or use a shunt with a well functioning valve like the Ahmed valve.

b) If there is wound leak post-operatively, or a large choroidal effusion, surgical treatment within 48 hours is indicated. During the 48 hours before surgery, a scleral shell[5], a bandage contact lens of 13 mm diameter or a giant contact lens of 22 mm diameter should be tried. These contact lenses provide resistance at the bleb site, which may allow reformation of the anterior chamber. The use of a contact lens can be combined with patching the eye.

c) A flat anterior chamber in a soft eye can be reformed after 48 hours at the slit lamp with viscoelastic through a paracentesis opening prepared during surgery. This should be undertaken only if the Seidel test is negative and no leak is detected through the incision site.

d) Large choroidal effusions associated with a flat chamber and soft eye should be drained, if the chamber does not reform following the above-mentioned procedures. Choroidal effusions that are not "kissing" can be watched for some weeks but "kissing" choroidals need to be drained speedily.



Avoid High Intraocular Pressure Post Op

It is not unusual to experience a hypertensive phase during the fourth to sixth post-operative week in the presence of an elevated bleb following filtration surgery. Increased IOP is treated with topical and systemic glaucoma medications, and the patient monitored throughout this period. In many cases, IOP will again decline after the sixth week. The role of **Laser Suture Lysis** as discussed in this Section is highly important at this stage (Figs. 1 and 2). However, if IOP remains at unacceptably high levels (over 30 mm Hg), more aggressive treatment is indicated. For example, in a Tenon's cyst type of bleb, fibrous tissue in the bleb can be broken down, using a 25-gauge needle, followed by bleb enhancement procedures, as will be described later in this Section (Figs. 1 and 2). If the hypertension is associated with a flat anterior chamber, the patient has "malignant glaucoma", and this needs to be treated surgically by the standard techniques.

Enhancement of Bleb Formation

Luntz points up that: 1) atraumatic dissection of conjunctiva and Tenon's fascia during the surgical procedure are most important to facilitate good bleb formation post-operatively.

2) Topical steroids[6] post-operatively in doses of up to one-hourly instillations are helpful; this can be slowly tapered and continued into the late post-operative phase (up to three months).

3) The use of enhancing agents, such as mitomycin or 5-FU[4] applied topically during surgery or 5-Fluorouracil by subconjunctival injection post-operatively. **Luntz** considers that an acceptable technique is to inject 10mg of 5-FU at the time of surgery subconjunctivally, and 10mg on alternate days post-operatively up to a maximum of 50mg. (**Editor's Note**: No specific dose is known or agreed to be the best. Dose varies according to different surgeon's experiences. It is clear, however, that although antimetabolites may be used in different dosages and frequency of administration, they are very effective in enhancing filtration).

4) Cutting the trabeculectomy flap sutures (where interrupted sutures have been used)[7] between the first and seventh post-operative day or, if mitomycin or 5-FU have been used, up to one month post-operatively, using the argon laser combined with ocular massage will generally produce a good bleb. The Hoskins lens is very useful for this purpose (Laser Suture Lysis, Figs. 1 and 2). Alternatively, if releasable sutures have been used as described in the technique for trabeculectomy (Chapter 18 and in Fig. 3 in this chapter), these can be removed one at a time by pulling on the corneal end of the suture and pulling the suture out.

5) Massage to the bleb, commencing between the first and 10th post-operative day, can continue late into the post-operative period.

Alvaro Moreno, M.D.,[9] emphasizes the importance of watching the filtering bleb in the immediate postoperative stage. If it is not formed we have to provoke its formation by pressing lightly on the globe 3 or 4 mm behind the superior limbus. The pressure is done with the thumb through the superior lid. This should be done under the slit lamp in order to make sure that the reformation of the bleb does not occur in a violent and exaggerated way which could provoke a sudden fall of the intraocular pressure with the consequent danger of inducing a flat chamber or hemorrhage in the posterior pole.

The patient should be examined every 24 to 48 hours to watch if the bleb has flattened again. If it does, the same maneuver may be repeated. If necessary, a reliable relative can be taught the maneuver of how to reform the bleb, so that the patient can have this massage at home for one minute 3 or 4 times a day. What is most important is to examine the patient very frequently until permanent drainage is established.

6) If the bleb appears to be fibrosing a needling procedure is indicated. (This technique is described in Chapter 30 - **Editor)**.

Laser Suture Lysis - Titrating Flow Through Sclerostomy

Hoskins et al[7] developed an additional use of the argon laser in filtration surgery by gradually releasing the trabeculectomy - flap nylon sutures with the laser and thereby titrating the IOP. (Figs. 1 and 2).

Indications

This procedure reduces the postoperative risk of hypotony, choroidal separation, and flat anterior chamber. The benefits of free flow through the sclerostomy at the scleral level are **obtained gradually** so that, in effect, we have both protection of a scleral-flap procedure and the benefits of a more free-flowing sclerostomy.

Technique for Laser Suture Lysis

The lamellar scleral flap is closed with interrupted 10-0 nylon sutures to maintain a formed anterior chamber postoperatively. The patient is observed postoperatively and pressures are taken serially, starting first postoperative day and continuing for three weeks. If intraocular pressure is higher than what is considered appropriate, the patient is brought to the argon laser for suture-lysis. (Figs. 1 and 2).

A Zeiss, Hoskins or Mandelkorn contact lens is used to obtain a good view of the suture and blanch the overlying conjunctiva.

After seeing the suture clearly, with the argon laser at a usual setting of 50 microns for a tenth of a second and with the power between 400 and 1,000 milliwatts (depending on the clarity of the suture tissue), the laser beam aims right at the suture and gives it one or two shots. The suture is released, separated, and spreads (Fig. 1) and the sclerostomy and scleral flap loosen (Fig. 2) augmenting aqueous flow through the sclerostomy. You can usually watch this happen right under your eyes. The conjunctiva is undisturbed and remains intact. One suture is released at a setting to titrate the intraocular pressure to the desired level.

Releasable Sutures

An alternative is to use releasable sutures for the scleral flap[8](Fig. 3). A scleral bite is taken in the posterior lip of the trabeculectomy scleral incision at the junction of the outer and middle third of the incision. The needle is then passed through the

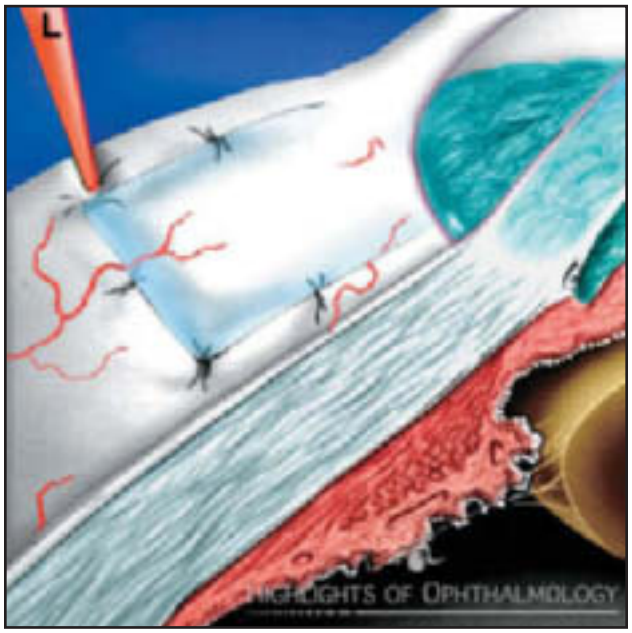


Fig. 1: Laser Suture Lysis Technique - Releasing the First Suture

Use either the Mandelkorn, Hoskins or Zeiss lens to obtain a good view of the suture and for blanching the overlying conjunctiva. With the argon laser (L) set at 50 microns for a tenth of a second and the power between 400 and 1,000 milliwatts, aim right at the suture and give it one or two shots. Here the suture is released at one corner of the scleral flap.

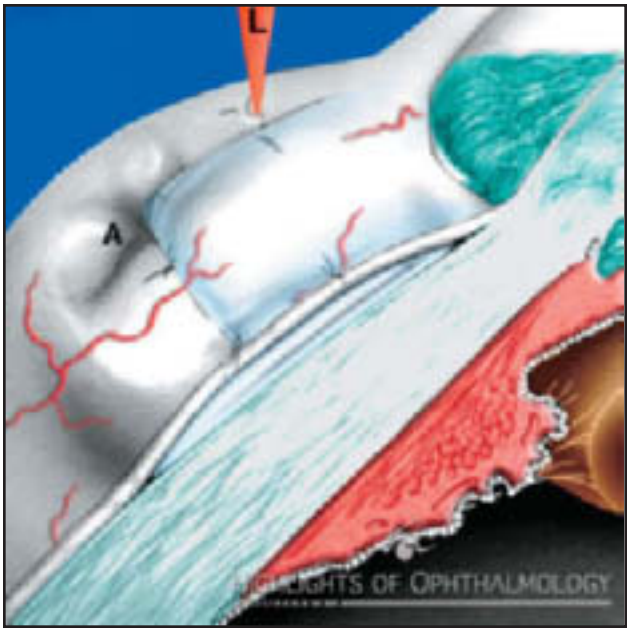


Fig. 2 (Above): Laser Suture Lysis Technique - Releasing Additional Sutures and Loosening the Scleral Flap

A second suture is broken, released, separated and spreads, and the sclerostomy and scleral flap loosen. Aqueous (A) flows into the subconjunctival space forming a bleb.

posterior corner of the lamellar scleral flap. The next bite is at the base of the cornea into corneal tissue, and another bite in the cornea parallel to the limbus (Fig. 3-A). The latter bite will prevent a windshield wiper effect when the suture is exposed on the corneal surface. Grasping the posterior end of the suture, which is attached to the posterior lip of the trabeculectomy incision, with tying forceps, three throws are made on the tying forceps, and the suture at the base of the cornea is grasped and pulled through the three loops (Fig. 3-B), forming a bow-tie suture, which is tightened into the posterior lip of the scleral flap (Fig. 3-C). The suture on the cornea is trimmed, leaving enough suture available to be grasped by forceps postoperatively. A similar suture is placed at the other end of the scleral flap. The configuration of the sutures is such that, when tightly tied, a central tunnel is formed (Fig. 3-C). This occurs because the suture through the posterior lip of the trabeculectomy is placed at the junction of the outer and middle third, whereas the suture in the posterior lip of the lamellar scleral flap is placed at the posterior corner of the flap. When these are tied, the edges of the flap are pulled inward to the junction of the outer and middle third of each side, forming a central tunnel, as indicated in the illustration.

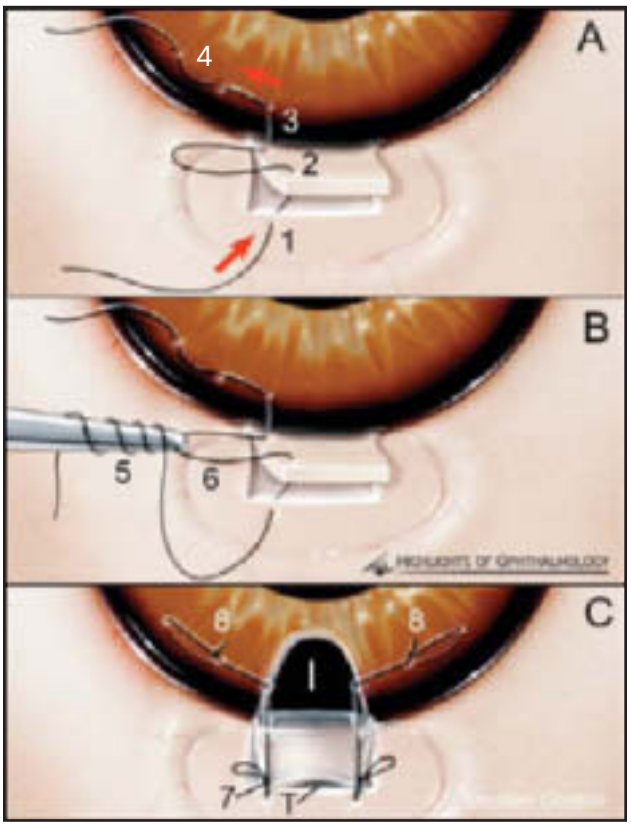


Fig. 3 (Right): Modified "Tunnel" Trabeculectomy Technique - Suturing Technique

The lamellar scleral flap is sutured with two or more releasable 10-0 nylon interrupted sutures. (A) A scleral bite is taken in the posterior lip of the trabeculectomy scleral incision at the junction of the outer and middle third of the incision (1). Next, the needle is passed through the posterior corner of the lamellar scleral flap (2). Then a bite is taken at the base of the cornea into corneal tissue (3) and then another bite in the cornea (4), parallel to the limbus. (B) To tie, the posterior end of the suture is grasped with tying forceps and three throws made (5). The suture portion at the base of the cornea is grasped and pulled through the three loops (6), forming a bow-tie suture. (C) This knot is tightened onto the posterior lip of the scleral flap (7). When this configuration is tied tightly on both sides of the scleral flap, a central tunnel (T) is formed. The suture ends on the cornea are trimmed (8). The conjunctival flap is then sutured to the sclera at the limbus with a continuous 10-0 nylon suture (not shown).

Pressure Control

Many surgeons today aim at reaching a pre-determined target tension they wish to achieve, as originally recommended by **Simmons**. **This target pressure is substantially lower than the pressure at which the patient was losing fields before surgery**. In **Simmons'** series with Laser Suture Lysis the average preoperative pressure was 25 mm Hg and the average final pressure was approximately 11.2 mm. The patients were **titrated** to a low protective pressure especially beneficial for advanced glaucoma and yet avoided the problems of early hypotony and achieved a free flow.

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9. Moreno, A : Personal communication

Chapter 30
NEEDLING PROCEDURE FOR FAILED OR FAILING FILTERING BLEBS

Craig H. Marcus, M.D.

The needling procedure in its various forms has evolved to salvage failed glaucoma filtering blebs caused by exuberant cicatrization including Tenon's cyst formation. Whether in a patient with recent or remote filtration surgery the goal is to avoid further intraoperative intervention and to reduce or eliminate medication. Although complications of in-office needling procedures parallel that of filtration surgery, they are an order of magnitude less in occurrence and needling is far more efficient than a repeat intraoperative procedure. The needling can be performed either in a minor procedure room or at the slit lamp if the surgeon is relatively ambidextrous. (**Editor's Note**: Some surgeons routinely use a minor procedure room or operating room because of the remote risk of post-procedure endophthalmitis.) Several techniques have been described and will be reviewed as well as the author's favored approach. For any skilled glaucoma surgeon the technique is easily mastered as long as careful planning and anatomical inspection are achieved. Additionally, a simple technique for salvaging impending failures of valved tube shunt surgery will be described.

Patient Selection

Patient selection is critical to the success of the procedure, especially if it will be performed at the slit lamp; since for the duration of the needling the patient must remain cooperative. With careful description of the procedure and preparation of the patient there is little difficulty maintaining concentration and positioning and with good technique there is virtually no discomfort.

The specific condition of the eye must also be well considered. Eyes that are overtly inflamed either from recent surgery or another cause should if at all possible be quieted first and needling delayed. Eyes with very thin avascular blebs or extremely scarred or thin conjunctiva should be avoided. Gonioscopy should be performed to examine the internal ostium in order to determine its size and patency. Special care must be taken in phakic eyes because of the added risk of cataract formation either from direct needle trauma or ensuing shallow or flat chamber.

Parameters for Success

The recent literature[1,2,3] identifies the parameters for a favorable outcome as 1) long-standing successful filtering blebs (the more remote the surgery the better); 2) fewer prior conjunctival incisions (reported in some but not all series); 3) those requiring only one needling (as opposed to multiple attempts); 4) an immediate post-needling pressure less than 10 mmHg;, and 5) possibly the use of adjunctive antimetabolite. Pre-needling intraocular pressure levels have been suggested in some but rejected in other series as a relevant factor.

The success of a needling procedure essentially depends on achieving three steps, namely: 1) lysing scar tissue or piercing Tenon's cyst; 2) ensuring an opened scleral flap; and 3) maintaining filtration into sub-Tenon's space.

Technique

After obtained consent and careful description the patient is given 2 successive drops of proparacaine and an antibiotic medication (alternatively povidone-iodine drops can be used). The periocular area is then carefully cleaned with betadine. A 1 cc syringe is used to draw-up a solution of 1% Xylocaine with 1:100,000 of epinephrine and then a 30 gauge needle is placed on it. Sterile balanced-salt solution (BSS) is then placed in a 3 cc syringe with a 25 gauge 5/8 inch needle. Then the patient is readied for the procedure.

At the slit-lamp the the patient is comfortably seated and a lid-speculum is gently placed in the eye. Goniosol solution is immediately placed on the cornea to keep it moist during the procedure with the patient in the downgaze position. A sponge to rest the surgeon's ipsilateral elbow is used along with low magnification of the slit lamp.

The 1 cc syringe is then used to enter into the sub-Tenon's space and balloon-up, blanch, and further anesthetize the conjunctival tissue 7-9 mm posterior to the limbus. Only 0.1 - 0.2cc of solution is needed (Fig. 1). Then the 25 gauge needle with the BSS is used to enter through the first needle tract. The conjunctiva tissue is hydrodissected toward the edge of the scleral flap as needed. Higher magnification is helpful here in order to more easily visualize the advancing needle tip and the flap. If only conjunctival scarring is present without flap adherence then BSS will be noted to circulate in the ante-



Fig. 1 The patient is seated at the slit lamp. A 1cc syringe fitted with a 30-gauge needle filled with Xylocaine 1% with 1:100,000 epinephrine enters the sub-Tenon's space 7-9mm posterior to the limbus. The solution is injected into the subconjunctival space, ballooning and blanching the overlying conjunctiva. Between 0.1 and 0.2cc of solution is used.

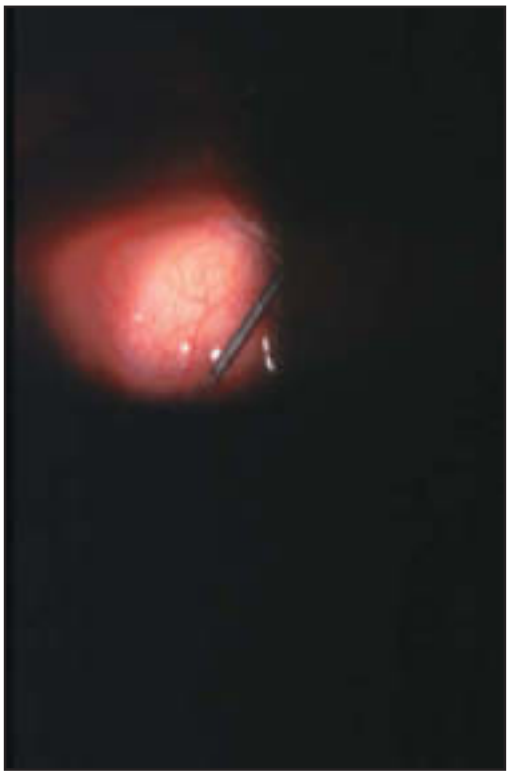


Fig. 2 A 25-gauge needle on a 3cc syringe filled with BSS is introduced through the same needle track as the 30-gauge needle used in Fig. 1. The 25-gauge needle is advanced toward the edge of the trabeculectomy scleral flap and, at the same time BSS is injected subconjunctivally to hydrodissect the conjunctiva as the needle advances towards the limbus.

rior chamber and one may stop here (Fig. 2). If flap adherence is anticipated or observed then the patient is asked to slowly and with a very small movement to look up (now nearly straight ahead). If the needle tip is right at the ostium no resistance into the anterior chamber should be encountered with a small advancement of the needle tip. Now the needle tip can be seen in the anterior chamber (Fig 3). Once this is achieved, the needle is withdrawn slightly back to the level of the edge of the flap and the needle is used to elevate it (Fig. 4). The beveled edge of the needle tip can be used to walk along the edge of the flap in order to ensure more complete lysis of adhesions. Next, the needle tip is placed above the plane of the flap and used to thoroughly hydrodissect the entire area surrounding the trabeculectomy site. The needle is then withdrawn.

The lid speculum is removed, antibiotic drops are instilled and the intraocular pressure is taken. If the pressure is above 10 mmHg the procedure is repeated immediately. If it is less than 10 mmHg the patient is instructed to use antibiotic drops and prednisilone acetate 1% every 1 -2 hours while awake and until seen the next day. A shield is worn at bedtime; however, no patch or shield is placed at the end of the procedure.

Before discharge the eye is reinspected at the slit lamp. Seidel testing usually will reveal a small leak at the needle entry site into the conjunctiva. Some advocate routine hand-held cautery of the leak at the needle entry site at the time of the procedure. However, within a 1 -2 days the leak usually closes

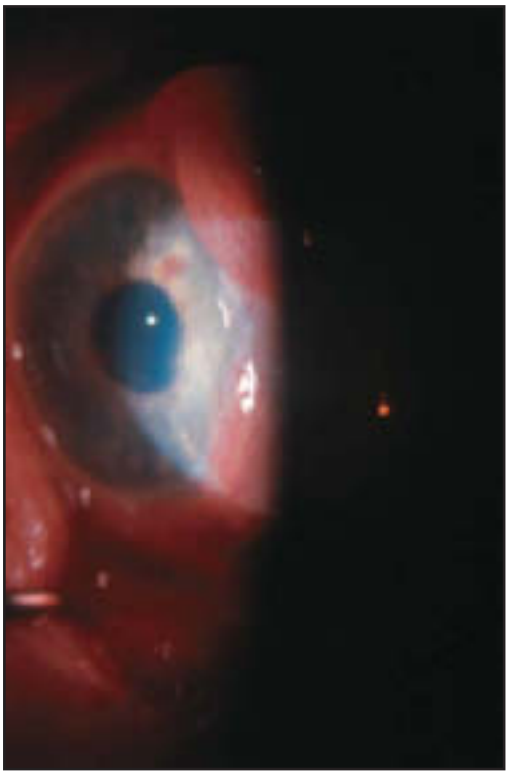


Fig. 3. The patient is asked to look up slowly until the needle reaches the edge of the trabeculectomy flap. If the trabeculectomy flap is open there will be no resistance to the needle entering the anterior chamber, as shown in this illustration.



Fig. 4. However, if the flap appears to be sealed, the needle tip is advance under the flap into the anterior chamber until the needle tip is visible in the AC. At this point, the needle is withdrawn to the level of the edge of the flap and is now used to elevate the flap.

without any significant flattening of the newly created bleb. If the leak persists beyond the first or second day then laser sealing of the needle tract is a good alternative. (Settings of 200-300 MW, 500 micron spot, 0.5 seconds with an argon laser is applied to the fluoroscein painted area identifying the leak.)

In the early post-needling period 5-fluorouracil can be injected as needed. An alternative technique has been advocated in one study: Mitomycin C (MMC) 0.1 ml of 0.4 mg/cc with 0.2 ml of Bupivacaine 15 - 20 minutes before the needling procedure. The success of the technique reported in this series; however, may not only be attributed to the adjunctive use of MMC, but also to the possible hypotensive effect of MMC, the multiple needling attempts for some the eyes in the series, or simply excellent technique. While the dose of MMC used in that series was carefully calculated to avoid any toxicity, one would advise caution in its use; and consider limiting its use to those cases with early bleb failure and attendant and exuberant inflammation.

Needling After Tube Shunt Surgery

In cases of tube shunt surgery with one-way valves (Ahmed, Krupin) (See Chapter 38 - **Editor**) that have impending failure a modified needling technique can be used to expand and maintain the bleb surrounding the plate. Here a 1 cc syringe with a 30 gauge needle is used. Hyaluronidase (Wydase) 0.2cc (30 Units), 0.1cc of Xylocaine, 0.2cc of 5-Fluorouracil (10 mg), and 0.2cc of air are drawn up into the syringe. Neither a speculum nor the slit lamp are needed. Anesthetic and antibiotic medication are instilled. A pledget of anesthetic and 2.5% phenylepherine is placed over the intended injection site. The needle pierces the conjuctiva and the bleb 10 mm posterior to the limbus directly over the explant and is directed tangentially in a posterior direction. The 0.5 cc of cocktail plus the trailing 0.2 cc of air (used to tamponade the mixture from escaping through the tiny needle track) is then injected. Usually, the intraocular pressure can be observed to decrease immediately. The eye then is examined at the slit lamp. No anterior chamber reaction is observed. Mild temporary lid swelling and even ptosis may be observed. Antibiotic medication is applied four times per day for several days and the patient followed serially.

Conclusion

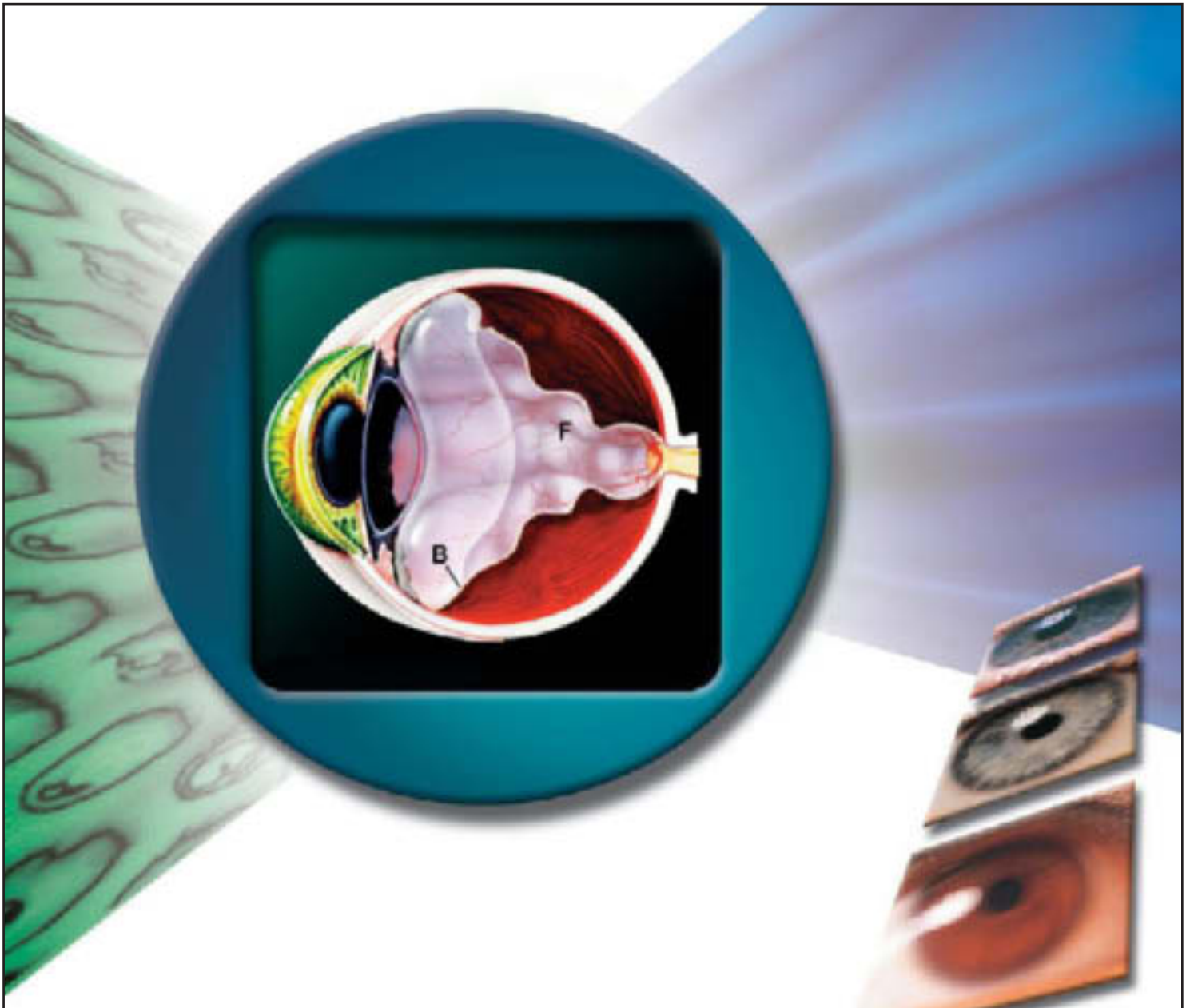
In summary, the needling procedure is an extremely efficient and effective method for salvaging a failed or failing filter. While its success rate may be slightly lower than an intra-operative procedure its reduced morbidity makes it an excellent addition to the glaucoma surgeon's armamentarium.

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SECTION VII

Management of Complications of Filtering Operations

Chapter 31
COMPLICATIONS OF GLAUCOMA FILTERING SURGERY

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Augusto Azuara-Blanco, M.D., Ph. D.

INTRAOPERATIVE COMPLICATIONS

A. Intraoperative Suprachoroidal Hemorrhage

Intraoperative suprachoroidal hemorrhage is a dramatic complication that can lead to loss of vision ("expulsive hemorrhage"). The incidence of suprachoroidal hemorrhage in glaucoma patients undergoing various types of intraocular surgery has been reported to be 0.73%. Risk factors include glaucoma, aphakia, previous vitrectomy, vitrectomy at the time of glaucoma surgery, buphthalmos, myopia, postoperative hypotony, arteriosclerosis, high blood pressure, tachycardia, and bleeding disorders. Nanophthalmos and Sturge-Weber syndrome have the highest risk for intraoperative suprachoroidal hemorrhage, which may occur in up to 30% of cases.

Intraoperative suprachoroidal hemorrhage can debut with sudden collapse of the anterior chamber, hardening of the globe, and prolapse of intraocular contents. The patient may experience pain breaking through the local anesthesia. A dark mass increasing in size can be observed through the pupil to evolve, but if the process is abrupt, the hemorrhage is more expulsive (i.e., ocular contents are expelled by the posterior pressure caused by the postretinal hemorrhage). (Fig. 1)

Treatment

Prompt and secure closure of the incision is the first goal of the treatment, with gentle reposition of prolapsed uvea. The surgeon's finger can be used to tamponade the incision site temporarily while

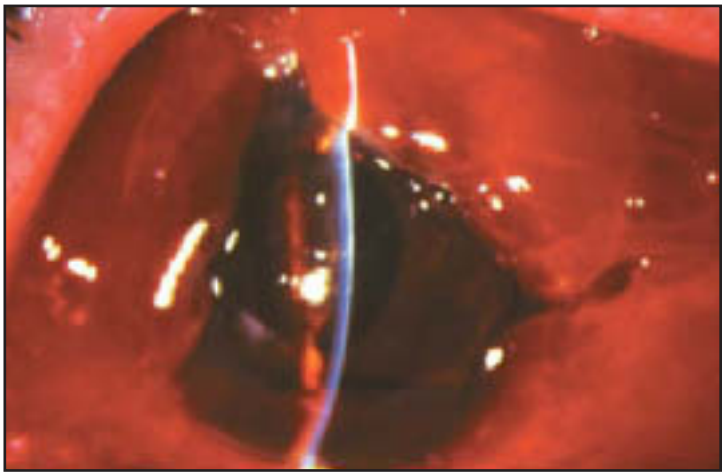


Figure 1 Large suprachoroidal hemorrhage with extension into the subconjunctival space following a trabeculectomy.

sutures are placed and until the expansion of the hemorrhage is stopped. Intravenous mannitol 20% (1-1.5 gr / kg) is administered. Once the wound is closed, the anterior chamber is reformed through a paracentesis. A conservative approach is recommended, although some authors propose immediate drainage of the hemorrhage through posterior sclerostomies (usually not possible because it rapidly clots). Prognosis for recovery of vision is uncertain but is better if the eye can be closed without loss of uvea and there is no intravitreal blood or retinal detachment.

Prevention

Several steps can be taken in "high risk" eyes: before surgery, correction of bleeding problems and discontinuation of inhibitors of platelet aggregation (e.g., acetylsalicylic acid) is recommended. Preoperative intravenous mannitol at the time of surgery has been recommended but is controversial. Prophylactic sclerostomies can be considered in high-risk eyes. Use of viscoelastic or an anterior chamber maintainer and tight suturing of the scleral flap to prevent hypotony are recommended. In very high risk eyes such as nanophthalmos and Sturge-Weber syndrome, prophylactic sclerostomies can be considered before starting the filtering procedure.

B. Limbal- vs. Fornix-based Conjunctival Flaps / Conjunctival Buttonholes

The type of conjunctival flap may influence the bleb morphology but has no influence on control of intraocular pressure. The theoretical advantages of the fornix-based conjunctival flap may include an improved exposure and access, a reduced risk of conjunctival button-hole formation, less trauma to Tenon's fascia, and the formation of a more posterior and diffuse bleb. However, with the fornix-based flap there is an increased risk of conjunctival wound leak in the early postoperative period if inadequately sutured. (Fig. 2)

Conjunctival buttonholes and tears can lead to hypotony, flat anterior chamber and failure of bleb formation. Buttonholes and tears are more likely to occur in cases with extensive conjunctival scarring. The usual cause for conjunctival buttonholes is penetration of the tissue by the tip of a sharp instrument or forceps (toothed forceps should be avoided). To rule out a conjunctival buttonhole, the conjunctiva should be carefully examined at the end of the procedure by filling the anterior chamber through the paracentesis and raising the filtering bleb.

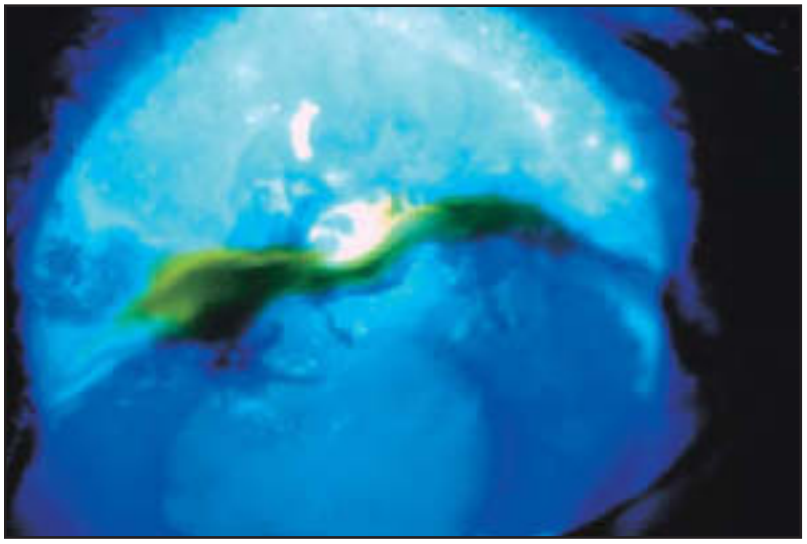


Figure 2 Fornix-based wound leak following trabeculectomy.

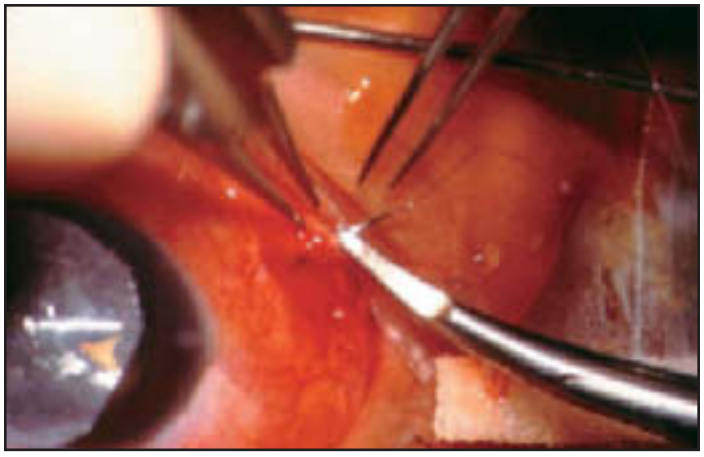


Figure 3 A buttonhole at the time of surgery requires closure with 10-0 nylon.

If detected, a conjunctival buttonhole should be closed with a "purse string" knot done either internally or externally with a 10-0 nylon on a rounded-body ("taper-point") needle. (Fig. 3) When the conjunctival buttonhole or tear occurs at the limbus, it can be sutured directly to the cornea, which may be de-epithelialized. A mattress suture or, if large, running or interrupted 10-0 nylon sutures can be used. When the buttonhole or tear occurs near the incised edge of a limbal-based conjunctival flap, it can be sutured to the wound.

C. Scleral Flap Disinsertion

A thin scleral flap can be torn or amputated from its base, or become incompetent if handling has been excessive. If a sclerostomy has not yet been performed, a new scleral flap should be dissected in a different area. If a sclerostomy has been already done, re-approximation of the scleral flap can be attempted with 10-0 or 11-0 nylon sutures. If unsuccessful, a patch graft of Tenon's capsule or a flap of partial thickness sclera from the adjacent area is necessary to cover the sclerostomy. Alternatively, donor sclera, fascia lata or pericardium (Tutoplast®) Innovative Opthalmic Products, Inc., Costa Masa, California, USA, can be used. (Fig. 4)

D. Vitreous Loss

Vitreous loss is uncommon, although it may happen in patients with previous trauma, aphakia,

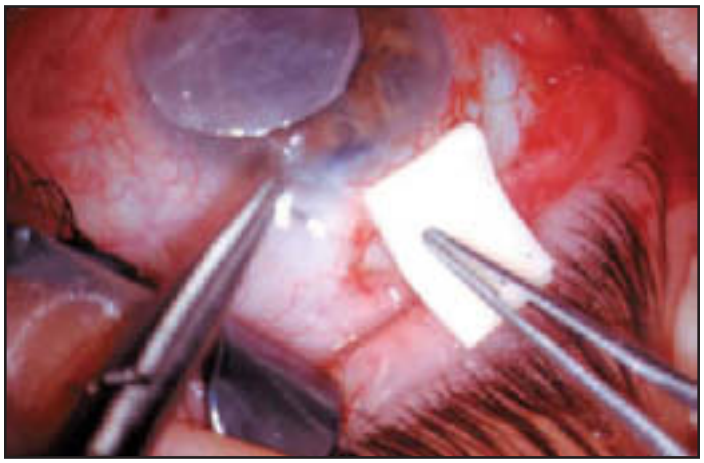


Figure 4 Tutoplast is used to cover a vigorous leak at the limbus.

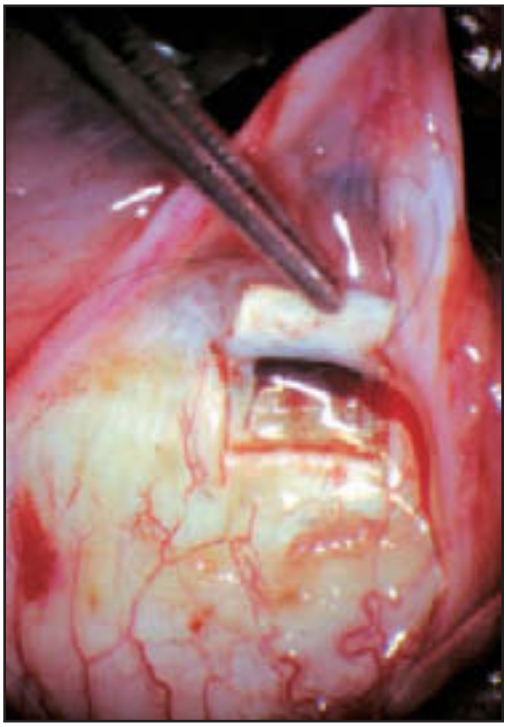


Figure 5 Following trabeculectomy, post-op hemorrhage usually occurs from the wound edge.

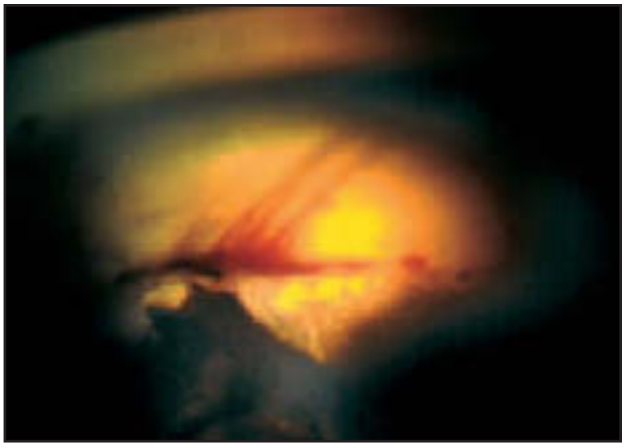


Figure 6 Gonioscopic view of bleeding from the wound edge.

buphthalmos, high myopia, a subluxated lens and severe pseudoexfoliation (Editor). Loss of vitreous can be associated with several complications and filtration failure. Vitreous should be removed from the surgical site and anterior chamber with a vitrectomy instrument.

Prevention

In aphakic eyes with vitreous filling the anterior chamber, an anterior vitrectomy can be planned as part of the primary procedure. In phakic or pseudophakic eyes with vitreous in the anterior chamber pars plana vitrectomy may be considered to adequately remove the vitreous from the posterior segment and to avoid lens/IOL subluxation and lens injury.

E. Intraoperative Bleeding and Hyphema

Bleeding commonly arises from the ciliary body or cut ends of the Schlemm's canal, although it might also arise from the corneoscleral incision or iris. (Fig. 5 - 6) Minimal bleeding usually stops spontaneously. If a bleeding spot does not stop, the source of hemorrhage should be identified and coagulated, with care to avoid lens injury. During filtration surgery bleeding is decreased by performing the internal sclerostomy as far anterior as possible.

Treatment

If hyphema is recognized postoperatively, in the vast majority of cases no treatment is necessary and the blood will be absorbed within a brief period of time. Cycloplegics, corticosteroids, restriction of activity, and elevation of head of the bed 30 to 45 degrees (to prevent blood from obstructing a superior sclerostomy) are recommended. Increased IOP can occur, particularly if the filtering site is obstructed by a blood clot, and it should be treated if necessary with aqueous suppressants. Surgical evacuation

is indicated depending on the level of IOP, size of hyphema, severity of optic nerve damage, likelihood of corneal blood staining, and presence of sickle trait or sickle cell anemia. Liquid blood can easily be removed with irrigation. If a clot has formed it can be removed by expression with viscoelastic or with a vitrectomy instrument set at low vacuum.

Prevention

Discontinuation of inhibitors of platelet aggregation pre-operatively is recommended. It is important to avoid opening the fistula too posterior (to avoid the iris root and ciliary body, which may cause excessive bleeding).

POSTOPERATIVE COMPLICATIONS DURING THE EARLY POSTOPERATIVE PERIOD

A. Hypotony and Flat Anterior Chamber - Choroidal Effusion

Hypotony after glaucoma surgery can be due to excessive aqueous outflow (overfiltration, wound leak or cyclodialysis cleft) or to reduced aqueous production (ciliochoroidal detachment, cyclodialysis cleft, inflammation, and use of aqueous suppressants). These conditions can coexist. For example, low IOP due to overfiltration or wound leak can induce cilio-choroidal detachment and secondary decreased aqueous production. Severe choroidal effusions are likely in nanophthalmus and choroidal hemangiomas, even without marked hypotony.

The clinical findings are related to the mechanism responsible for ocular hypotony. At the slit-lamp examination the anterior chamber depth and certain bleb characteristics should be assessed. When there is a conjunctival buttonhole and leak, the bleb is usually flat (see below); when the filtration is excessive and without leak there is an elevated bleb. (Fig. 7)

The severity of flat anterior chamber can be classified according to George L. Spaeth as grade I, when there is peripheral-iris apposition, grade II, (Fig. 8) with pupillary border-corneal apposition, or

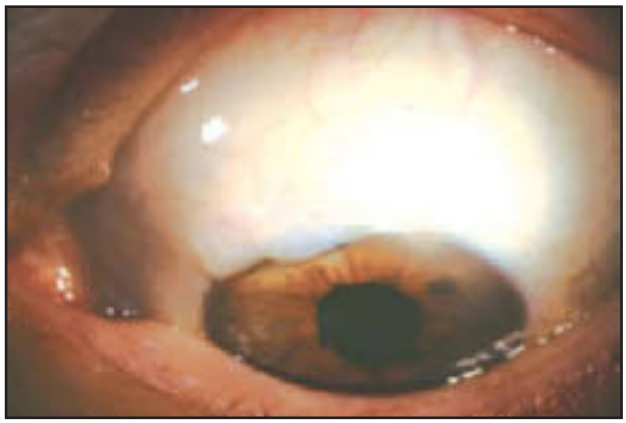


Figure 7 Large bleb with excessive filtration.

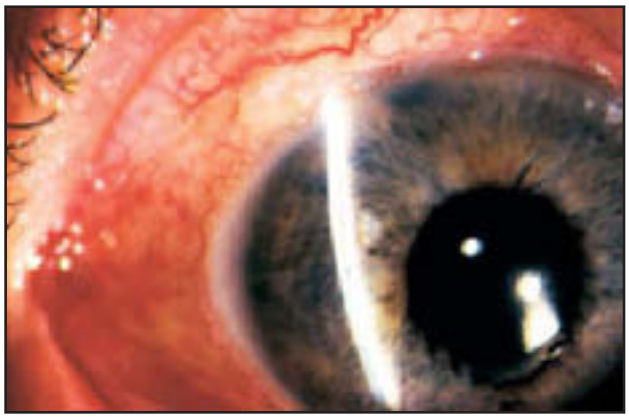


Figure 8 Grade II flat chamber with peripheral-iris apposition.

grade III, with lens-corneal touch (Fig. 9). The central anterior chamber depth can be also described relative to the corneal thickness.

Hypotony in the early postoperative period can be associated with several complications. Fortunately, most cases are resolved with postoperative treatment allowing for preservation of the bleb function. Hypotony can induce cilio-choroidal detachment (Fig. 10) (visible as mound-like elevations of the choroid, more commonly seen in the periphery), decreased aqueous production, gradual failure of the bleb, cataract, corneal edema or suprachoroidal hemorrhage. Corneal edema and Descemet's membrane folds are typically present.

Treatment

The initial management of early postoperative hypotony with a formed or shallow anterior chamber is conservative. Topical steroids and cycloplegics are used. Restrictions in activity (bending, weight lifting) and avoidance of Valsalva-positive conditions are recommended, especially in patients at risk for suprachoroidal hemorrhage. If there is hyposecretion related to intraocular inflammation and/or ciliochoroidal detachment the initial treatment consists of intense corticosteroid therapy and long-acting cycloplegics that stabilize the blood-aqueous barrier. Tight closure of the scleral flap is recommended when there is a high risk of postoperative hypotony (Fig. 11).



Figure 9 Grade III flat anterior chamber with lens-corneal touch.

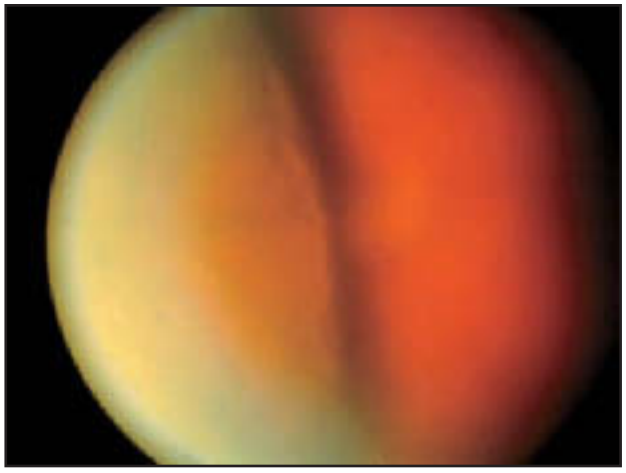


Figure 10 Large cilio-choroidal detachment with mound-like elevation of the choroid.

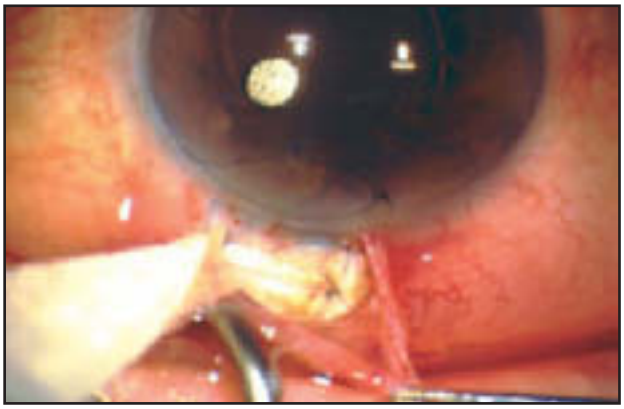


Figure 11 Tight closure of the scleral flap. This is recommended when there is a high risk of post-operative hypotony.

Intervention is indicated in cases with hypotony associated with other complications (e.g., flat anterior chamber, bleb leak), and in eyes with persistent low IOP with loss of visual acuity and hypotony maculopathy. (Fig. 12) Treatment should be aimed at correcting the specific cause of hypotony. The use of pressure patching, a 20-22 mm therapeutic soft contact lens (Fig. 13) or a Simmons' shell (Fig. 14) may be beneficial in cases of hypotony due to excessive filtration by tamponading the filtration site that allows gradual improvement in the anterior chamber depth. The Simmons shell is a 22 mm dome-shaped shell of transparent polymethylmethacrylate. A raised platform on the concave inner surface of the shell is positioned over the sclerostomy site. The curvature is designed to selectively indent the perilimbal area when pressure dressing is applied. The Simmons shell is usually effective but it may be uncomfortable, tonometry is not possible to monitor the IOP, decentration of the shell is frequent unless sutured to the conjunctiva, it requires close (daily) monitoring, and corneal complications (epithelial defects and abrasions) are common. A bandage contact lens is required. It is particularly difficult for monocular patients, and overall the use of Simmons' shell is obsolete. A therapeutic soft contact lens is preferable.

When there is lens-corneal touch (flat anterior chamber, grade III) immediate surgical intervention is necessary to prevent endothelial damage and

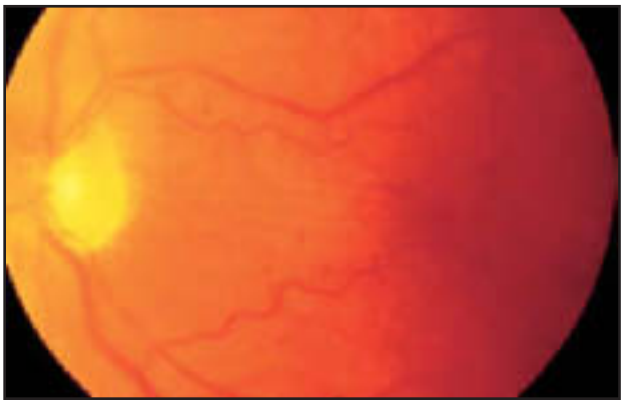


Figure 12 Hypotony with striae through the macula.



Figure 13 Large bandage lens (Kontourtm 22 mm in length).



Figure 14 Simmons compression shell, placed over the filtering bleb.

cataract formation. Reformation of the anterior chamber with air, balanced salt solution or preferably by a viscoelastic can be done at the slit lamp or under the operating microscope through the paracentesis made intraoperatively. Viscoelastic material is best for maintaining, at least temporarily, the anterior chamber depth. If the flattening recurs, surgical intervention to address the cause of flat anterior chamber is required. When there are large and appositional choroidal effusions drainage of the fluid is also necessary.

Surgical drainage of choroidal effusions may be prudent in cases with persistent iridocorneal apposition and/or massive choroidal effusions with apposition of retinal surfaces within the macular area. (Fig. 15) A sclerostomy is performed in one or occasionally in both inferior quadrants, and a tangential incision is performed in the sclera 4 mm posterior to the limbus. An infusion line can be connected to an anterior chamber maintainer through the paracentesis to maintain a deep anterior chamber while the choroidal effusion is evacuated. It is usually necessary for the surgeon to hold the sclerotomy open with forceps to facilitate drainage. A 1mm cyclodialisis spatula can be introduced into the suprachoroidal space if the choroidal effusion is thought to be loculated. Indirect ophthalmoscopic examination after drainage confirms flattening of the choroid. The sclerostomy site is closed with 7-0 Vycril, and the conjunctiva is closed watertight.

In very high risk eyes such as nanophthalmos and Sturge-Weber syndrome, prophylactic sclerostomies can be considered before starting the filtering procedure, and left open.

B. Early Wound or Bleb Leak

Wound and bleb leaks are detected with the Seidel test. A wet fluorescein strip is applied to the inferior tarsal conjunctiva or, very gently, directly to the wound and bleb. Without applying pressure, the eye is examined under cobalt blue illumination. If there is a leak unstained aqueous humor will be seen flowing into the tear film. (Fig. 16) If there is no spontaneous leakage pressure may be gently applied to the globe or to the bleb while the suspicious area is examined.

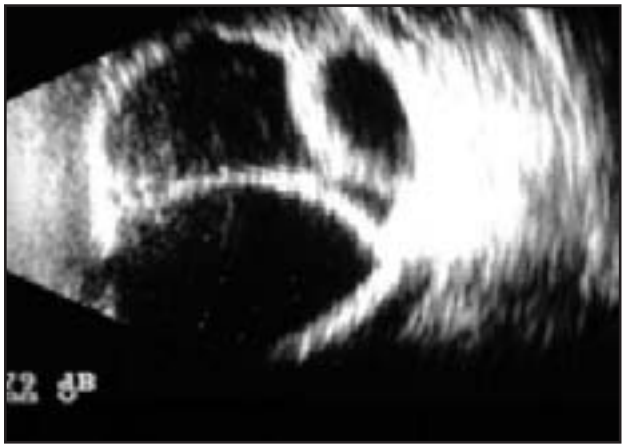


Figure 15 Large cilio-choroidal detachment with kissing choroidals and apposition of retinal surfaces.

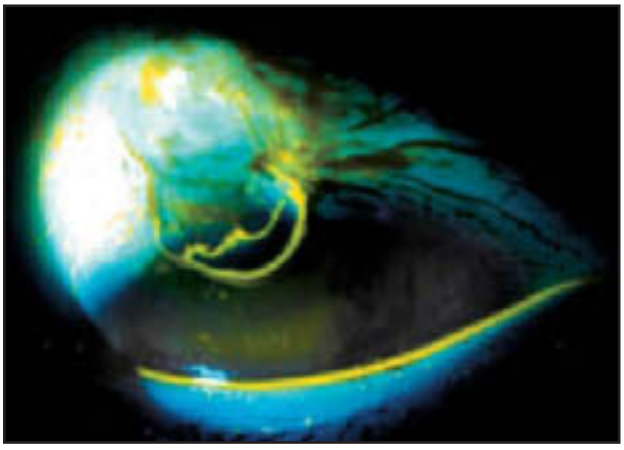


Figure 16 Seidel positive bleb, responsible for the IOP of 3 mm Hg.

Small leaks around sutures often close without treatment. If there is a brisk leak, pressure patching or a large diameter (16-20 mm) soft therapeutic contact lens can be can be tried for 24 to 48 hours, or a 72-hour collagen (porcine) shield. Broad spectrum topical antibiotics should be administered to protect against infection, and close observation is mandatory. Fibrin tissue glue is a mixture of fibrinogen and thrombin which induces the formation of a clot that can seal bleb leaks. It is a non-irritating procedure that requires no patching. Tisseel (Immuno AG Industriestr, Vienna), is a commercialized fibrin glue, not FDA approved, that has the disadvantage of being prepared from pooled plasma and thus may have the potential risk of transmitting blood-borne pathogens. Autologous fibrin tissue glue (AFTG) is prepared from the patient's blood, therefore eliminating the risk for disease transmission. Cyanoacrylate glue (Histo-acryl, B.Brown Melsungen) (Fig. 17) adheres to tissues and can effectively close an early wound bleb leak seen shortly after surgery. The glue must be applied to a dry conjunctival surface, and only a small amount of glue should be used. The use of a bandage contact lens can prevent the adhesive from being dislodged. (Fig. 18) Suturing technique or wound leaks or buttonholes was described above.

C. Suprachoroidal Hemorrhage

Postoperative suprachoroidal hemorrhage usually occurs within the first week after glaucoma surgery (most commonly during the first three days) and is usually associated with postoperative hypotony. Risk factors were described above (see Intraoperative suprachoroidal hemorrhage). Valsalva maneuvers may trigger the choroidal hemorrhage.

The development of a suprachoroidal hemorrhage is typically acute and associated with the sudden onset of severe pain and decrease in vision. Examination of the anterior segment frequently reveals a shallow anterior chamber and a normal or high intraocular pressure. On fundus exam a detached and dark choroid is noted. The choroidal elevations have a dark reddish brown color. Some cases present bleeding into the vitreous cavity and, uncommonly, retinal detachment. Ultrasonography



Figure 17 Cyanoacrylate glue which adheres to the tissue to effectively close an early wound bleb leak.

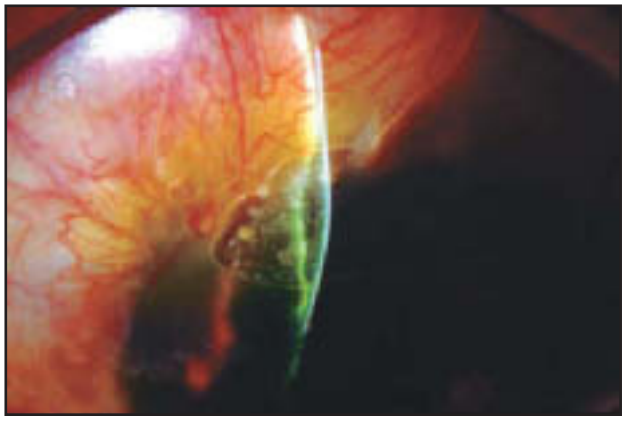


Figure 18 Use of a bandage contact lens can prevent the adhesive from becoming dislodged.

can be used to diagnose suprachoroidal hemorrhage when fundus exam is not possible.

Treatment of postoperative suprachoroidal hemorrhage is directed toward control of the IOP and relief of pain. The majority of small to medium-sized hemorrhages resolve spontaneously over subsequent weeks. Bleeding into the vitreous cavity at the time of the hemorrhage, and retinal detachment greatly worsen the visual prognosis. The indications for drainage include intolerable pain, a persistent flat anterior chamber, and massive "kissing" choroidal detachments (see below) (Fig. 15). A waiting period of about two weeks following a suprachoroidal hemorrhage is advised for the fibrinolytic response to liquefy the clot, which may be confirmed by B-scan ultrasound.

Prevention. The patient is urged to restrict activities (bending, weight lifting) and to avoid Valsalva-positive conditions (constipation, vigorous coughing, sneezing or nose-blowing or straining at stool – Editor) during the early postoperative period. Postoperative hypotony should be avoided in high risk eyes.

D. Aqueous Misdirection

Aqueous misdirection or "malignant glaucoma" or "ciliary block glaucoma" is characterized by a shallowing or flattening of the anterior chamber (Fig. 19) even in the presence of a patent iridectomy and absence of chorioretinal pathology (such as suprachoroidal hemorrhage), commonly with an accompanying rise in intraocular pressure (IOP). The chance of developing malignant glaucoma is greatest in phakic hyperopic (small) eyes with angle closure glaucoma. It occurs in 2% to 4% of patients operated on for angle closure glaucoma.

In this condition aqueous is diverted posteriorly towards the vitreous cavity and trapped in the vitreous cavity, increasing the vitreous volume and shallowing the anterior chamber. Small choroidal effusions and shallow anterior chamber sometimes occur before the episode of aqueous misdirection. In some cases pupillary block occurs first and is followed by aqueous misdirection. (Fig. 20)

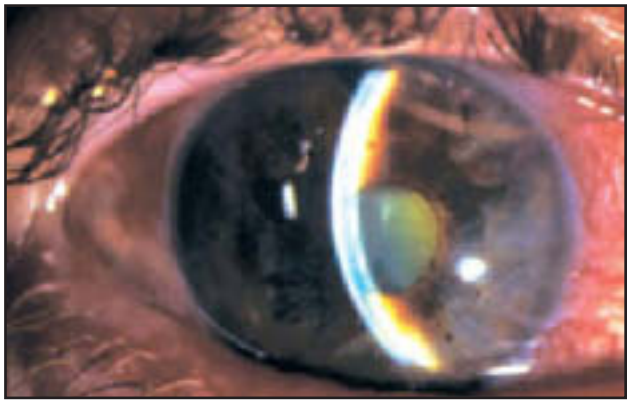


Figure 19 Aqueous misdirection in a phakic hyperopic eye.

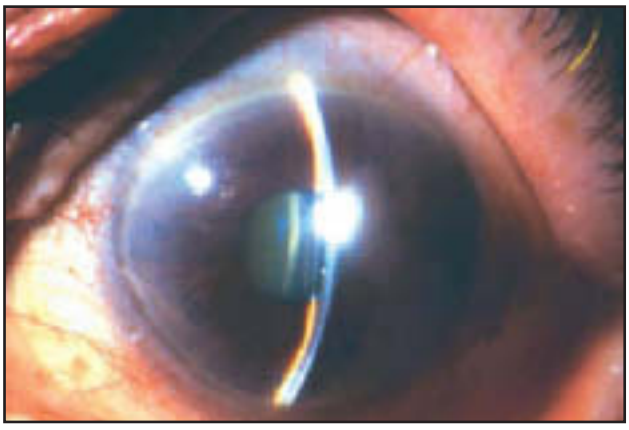


Figure 20 Pupillary block with an extremely shallow anterior chamber and elevated IOP. No iridectomy is present.



Figure 21 Malignant glaucoma or aqueous misdirection following a trabeculectomy with a Grade II flat anterior chamber.

Aqueous misdirection usually occurs in the early postoperative period after filtration surgery. (Fig. 21) The anterior chamber is shallow and the intraocular pressure is commonly high. However, with a functioning filtration bleb the intraocular pressure may be within normal limits. If the adequacy of the surgical iridectomy is in doubt and pupillary block is possible, a laser iridotomy should be performed.

Medical treatment, laser and vitreous surgery have all been useful options to treat aqueous misdirection. This condition is initially managed with mydriatic-cycloplegic drops, aqueous suppressants and hyperosmotics. Topical 1% atropine or 1% cyclopentolate four times daily and 2.5% phenylephrine four times daily are used. These agents hopefully will result in a posterior movement of the lens-iris diaphragm. In cases of aphakic aqueous misdirection, mydriatic-cycloplegic drops are of little benefit. However, it is reasonable to use them for their effect on relaxation of the ciliary body muscle. Systemic carbonic anhydrase inhibitors and topical beta-adrenergic blocking agents in full doses are important. Osmotics (isosorbide, glycerin, or intravenous mannitol) can be also very helpful to decrease the fluid content of the vitreous cavity, and can be repeated after 12 hours with cautious control of electrolytes, hydration, and possible systemic complications. If it is well tolerated and there are no contraindications, the medical treatment is tried for 2-4 days. If the condition is relieved (i.e., the anterior chamber has deepened), the hyperosmostic agents are discontinued first, and the aqueous suppressants are reduced or even stopped over several days. Phenylephrine drops can be stopped, but the cycloplegic drops can be continued for months. Medical treatment relieves about 50% of cases of aqueous misdirection.

If medical therapy is unsuccessful and the ocular media are clear, a Nd:YAG laser capsulotomy and hyaloidotomy is used to disrupt the anterior vitreous face in pseudophakic and aphakic cases. The initial laser energy is between 2 and 4 millijoules. The focus is placed posterior to the anterior hyaloid. After a successful Nd:YAG hyaloidotomy a slight deepening is usually seen, which increases over the next hours. In pseudophakic eyes, a peripheral hyaloidotomy is more efficient than a central hyaloidotomy because the lens capsule and intraocular lens can prevent communication between the vitreous cavity and the anterior chamber. In phakic eyes, Nd:YAG hyaloidotomy can be tried through the peripheral iridectomy, focusing behind the zonules but in front of the ciliary body. However, a clear view and sharp focusing may not be possible, and there is a risk of lens or zonular injury.

Pars plana vitrectomy can be considered when other therapies fail. A standard 3-port pars plana vitrectomy, removing the anterior vitreous and part of the anterior hyaloid, is done. In phakic patients, the lens can sometimes be spared, but the probability of recurrence is higher. Pars plana tube-shunt insertion with vitrectomy has been recommended to treat patients with aqueous misdirection, especially in cases with angle closure glaucoma. The implantation of the tube shunt through pars plana can help prevent recurrence of this condition and can help in long-term control of IOP. (A large patent peripheral iridectomy or multiple peripheral iridectomies must be in place – **Editor**).

Alternatively, phakic eyes that do not respond to medical therapy and pars plana vitrectomy can be successfully treated with phacoemulsification of the lens, posterior capsulectomy and anterior vitrectomy. In pseudophakic eyes a vitreous cutter can be introduced through the anterior chamber through a paracentesis, associated with an anterior chamber maintainer. The vitreous cutter is used to enlarge the peripheral iridectomy and then is directed posteriorly to do a localized zonulo-hyaloido-vitrectomy (Lois' technique).

Prevention: In high risk eyes undergoing filtration surgery the decompression and shallowing of the anterior chamber should be minimized. The use of viscoelastic and a large peripheral iridectomy can be helpful. Because aqueous misdirection can occur during filtration surgery, eyes with intraoperative shallow anterior chamber and high IOP should be treated promptly with intraoperative mannitol and cycloplegics. Tight suturing of the scleral flap is also needed. Aqueous suppressants should be also considered.(Vitrectomy should be considered – Editor).

Postoperative overfiltration should be avoided with a thick scleral flap sutured tighter and with more sutures than usual. (Fig. 11) Postoperatively, judicious suture lysis or cutting/pulling releasable sutures and slow tapering of cycloplegics are recommended. A postoperative shallow anterior chamber due to overfiltration should be vigorously treated.

E. Pupillary Block

Pupillary block can be caused by adhesions between the iris and lens, pseudophakos, or vitreous. The inability of aqueous humor to pass from the posterior to the anterior chamber results in the forward movement of the peripheral iris and closure of the drainage angle. Pupillary block typically occurs as a flat or shallow anterior chamber with normal or elevated pressure. It may be difficult to distinguish from malignant glaucoma. (or it may be considered as part of the clinical spectrum of malignant glaucoma – **Editor**).

Although a peripheral iridectomy is intended at the time of filtration surgery, in a few cases only the stroma of the iris is removed and the posterior pigment epithelium is left intact. In these cases blockage may develop. In other cases the iris may become incarcerated in the wound, or the iridectomy may be obstructed by intraocular tissue, such as Descemet's membrane, anterior hyaloid surface, vitreous (in aphakic eyes), or ciliary processes. If the IOP is high and the anterior chamber is flat after a patent peripheral iridectomy has been confirmed, malignant glaucoma should be considered.

Therapy with cycloplegic-mydriatics may resolve pupillary block but a Nd:YAG peripheral iridotomy should be done. The anterior chamber will readily deepen after iridotomy is performed, although in presence of localized compartments of blockage multiple iridotomies are necessary. This deepening is usually associated with the sudden escape of aqueous humor through the iridectomy and confirms the diagnosis of pupillary block. If laser iridotomy cannot be completed a surgical iridectomy should be done.

F. Early Failure of Filtering Bleb

Early failure of filtering blebs is characterized by a high IOP, deep anterior chamber and low filtering bleb. (Fig. 22) A tight scleral flap and episcleral fibrosis are the most common causes of early bleb failure. Internal obstruction of the fistula by blood clot, vitreous, iris, or incompletely excised Descemet's membrane is also possible.

Failing blebs should be recognized promptly because if obstruction is not relieved permanent adhesions between conjunctiva and episclera can lead to failure of the bleb. The most important period is between the first and fourth weeks, when the inflammatory response is maximal.

Complications associated with the use of postoperative 5-FU include corneal and conjunctival epithelial toxicity, (Fif. 23) corneal ulcers, (Fig. 24) conjunctival wound leaks, subconjunctival hemorrhage, or inadvertent intraocular spread of 5-FU. The frequency of complications is reduced with lower dosages of 15 - 50 mg administered in 3 -10 injections, each of 5 mg, according to individual response. Mitomycin-C is approximately 100 times



Figure 22 Failed bleb shortly after fornix-based trabeculectomy.



Figure 23 Confluent SPK following 5-FU injection.

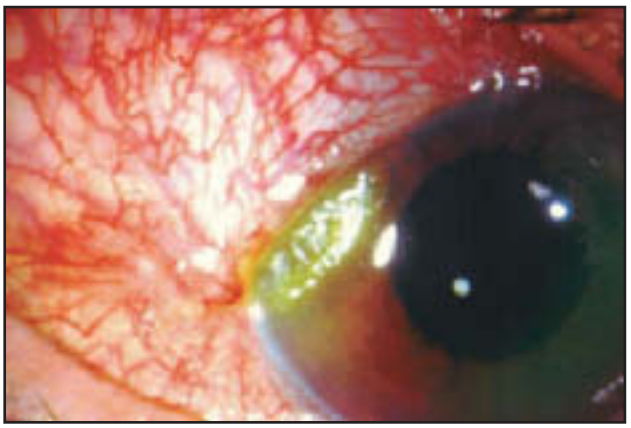


Figure 24 Dellen following trabeculectomy with 5-FU.

more potent than 5-FU. Postoperative complications associated with overfiltration, hypotony maculopathy, bleb leak, and bleb-related ocular infections are more likely to occur when mitomycin-C is used.

During the first few days, digital ocular massage and focal distortion of the scleral flap can be used to temporarily improve the function and elevate the filtering bleb. Digital ocular compression (DOC) can be applied to the inferior sclera or cornea through the inferior eye-lid, or to the sclera posterior to the scleral flap through the superior eye-lid. Focal compression is applied with a moistened cotton tip or blunt instrument at the edge of the scleral flap.

Laser suture lysis can enhance the filtration during the early postoperative period. The timing of suture release is critical. Suture lysis is effective within the first two weeks after surgery without antimetabolites; later, fibrosis of the scleral flap may negate any beneficial effect of this procedure. If antimetabolites have been used at the time of surgery suture lysis can be effective several weeks after surgery. Specially designed lenses such as Hoskins, Ritch or Mandelkorn lens, the central button edge of the Zeiss and Sussman lenses, the Goldmann lens, glass rods or glass pipettes can be used. After the suture is cut, if the bleb elevates, (Fig. 25) no additional sutures need to be cut. If the bleb and IOP are unchanged, ocular massage or focal pressure can be applied and, if there is no change in the bleb, another suture should be cut. When there is subconjunctival hemorrhage krypton red or a diode laser should be used because their wavelengths are least absorbed by blood.

Releasable sutures (Fig. 26) are as effective as laser suture lysis. The externalized sutures are easily removed and are effective in cases of hemorrhagic conjunctiva or thickened Tenon's tissue (that would make difficult suture lysis). The disadvantages of releasable sutures include the need for additional intraoperative manipulation and possibly increased risk of ocular infection. Several techniques have been described (see Section on Trabeculectomy for description of releasable sutures).

If these procedures fail then the bleb can be needled (see Table on "Needling of Filtering Bleb").(**Editor's Note**: See also chapter 30).

When the cause of filtration failure is a blood clot or fibrinous clot (Fig. 27) occluding the sclerostomy tissue plasminogen activator (tPA) can be helpful. Recombinant tPA is a protease with clot-specific fibrinolytic activity. It can be injected into the anterior chamber or subconjunctivally and the dosage is 7-10-micrograms in 0.1 ml. It works rapidly so that within 3 hours the effect is usually apparent. Hyphema is the most frequent complication, and tPA should be consider only if there is no active or recent bleeding. Alternatively, the blood clot can be dispersed by exposing it to Nd:YAG laser with settings at 1.5 to 2.0 mJ power via a gonioscopic lens.



Figure 25 Bleb elevation after laser suture lysis.



Figure 26 Releasable sutures tied into clear cornea at the time of trabeculectomy surgery.

TABLE
Needling of Filtering Bleb

1. The procedure can be done at the slit lamp or in the operating room
2. Topical anesthesia is used. A cotton pledget can be soaked in the anesthetic and applied to the area of injection. Topical phenylephrine 2.5% is used to vasoconstric the conjunctival vessels (optional).
3. Povidone-iodine 5% solution is applied to the conjunctiva, eyelid margins, eyelashes and eyelids.
4. A lid speculum can be used (optional).
5. On a tuberculin syringe a 30- or 27-gauge needle penetrates the conjunctiva, 5 to 10 mm from the scleral fistula (through conjunctiva not treated with an antifibrosis regimen).
6. Balanced salt solution or lidocaine can be injected to raise the conjunctiva (optional).
7. The needle is then advanced into the bleb cavity and beneath the scleral flap. A sweeping motion or to and fro movements is done with the edge or the tip of the needle, respectively.
8. "Aggressive alternative": the needle can be advanced through the internal ostium (optional) until the needle is visualized in the anterior chamber (this procedure should be done with extreme caution in phakic eyes).
9. Then end point is elevation of the bleb rises IOP reduction.
10. A Seidel test should be done to evaluate wound leaks through the conjunctival entry point, which can be cauterized.
11. Postoperatively, topical antibiotics and steroids are used, with or without additional injections of 5-FU.

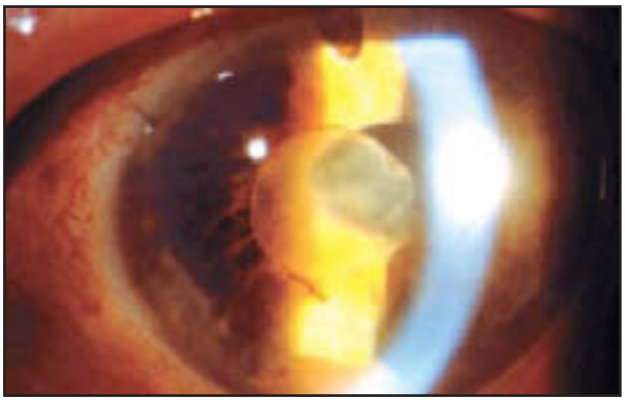


Figure 27 Fibrinous clot in the anterior chamber following glaucoma filtering surgery.

Encapsulated Blebs

Encapsulated blebs, also called Tenon's cysts, are localized, elevated and tense filtering blebs, with vascular engorgement of the overlying conjunctiva and a thick connective tissue. (Fig. 28) This type of bleb commonly appears within 2 to 6 weeks following surgery. Encapsulation of the filtering bleb is associated with a rise of IOP after an initial period of pressure control following glaucoma surgery. They can interfere with upper lid movement and tear film distribution leading to corneal complications such us dellen (Fig. 24) and astigmatism. Often it is seen through the eyelid simulating a lid mass.

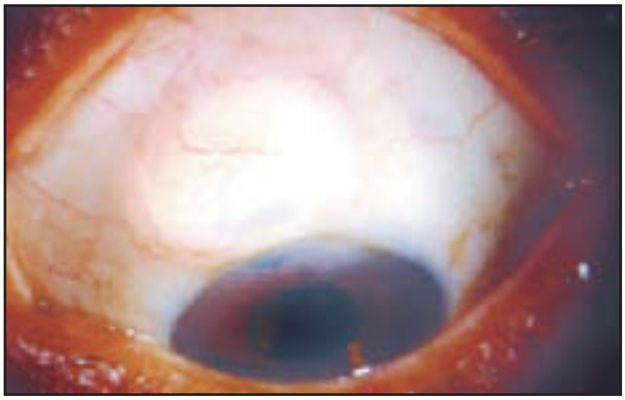


Figure 28 Encapsulated Tenon's cyst with high tight bleb, IOP 36 mm Hg.



Figure 29 Tight Tenon's cyst 6 weeks following trabeculectomy with 5-FU, IOP 41 mm Hg.

The frequency of bleb encapsulation after trabeculectomies without antimetabolites ranges from 8.3% to 28%. In trabeculectomies with postoperative 5-FU the incidence has been frequently reported higher. (Fig. 29) The frequency of encapsulated blebs after guarded filtering procedures with mitomycin-C is lower. Predisposing factors may include male gender, glove powder, and prior treatment with sympathomimetics, argon laser trabeculoplasty, and surgery involving the conjunctiva. The long-term prognosis for IOP control in eyes that develop encapsulated bleb is relatively good.

Initial management of encapsulated blebs include antiglaucoma medications in cases of elevated IOP, topical steroids, and digital massage or focal compression of the bleb. Deciding between conservative management (medical) or a surgical revision is usually dependent upon the severity of glaucomatous damage, the level of IOP, and the response to medical management. When surgical revision is needed the simplest technique is to cut the fibrotic wall with a 27-gauge needle or a Ziegler knife. This procedure can be done at the slit-lamp and, if effective, restores aqueous outflow to a larger subconjunctival area. Subconjunctival injections of 5-FU for two weeks after bleb revision increases the chances of success. Alternatively, 0.1 ml of mitomycin-C (0.4 mg/ml) diluted in 0.1 ml of non-preserved lidocaine can be used 30 minutes prior to needling. This latter option is currently under investigation. Excision of the fibrotic tissue has been also proposed.

G. Visual Loss

Unexplained loss of central visual field (i.e.,"wipe out") after glaucoma surgery is rare. Older patients with advanced visual field defects affecting the central field, with split fixation, are at increased risk. Early undiagnosed postoperative IOP spikes and severe postoperative hypotony have been suspected causes for "wipe-out".

POSTOPERATIVE COMPLICATIONS OCCURING MONTHS-YEARS AFTER SURGERY

A. Hypotony Maculopathy Due to Overfiltration

Chronic hypotony after filtration surgery is most commonly due to overfiltration Some patients with persistent hypotony develop loss of central vision secondary to marked irregular folding of the choroid and retina. Initially, these folds are broad and not sharply delineated. They tend to radiate outward in a branching fashion temporally from the optic disc, and concentrically or irregularly nasally to

the disc. There may be swelling of the peripapillary choroid simulating papilledema. The retina often shows a series of stellate folds around the center of the fovea. The retinal vessels are tortuous and sometimes engorged. (Fig. 30) Early detection of this condition is important because correction of the cause will usually result in visual improvement. In cases of prolonged hypotony permanent pigmented lines, caused by changes in the retinal pigment epithelium, occur in the macular area and nasally.

The incidence of hypotony maculopathy after glaucoma surgery has increased with the use of antifibrotic agents, specifically mitomycin-C. A direct toxic effect of mitomycin cannot be ruled out. The maculopathy is most likely to occur in young myopic patients, who may have a sclera less rigid and more susceptible to swelling and contraction. Injection of autologous blood into the bleb to reduce overfiltration or to treat bleb leaks after filtering surgery has been reported. Inflammatory cells and serum proteins from the injected blood may accelerate the inflammatory and healing process, which decreases filtration. Approximately 0.2 to 0.5 ml of venous blood from the patient's arm (extracted with a 25-gauge needle in a tuberculin syringe) are injected into and around the filtering bleb with a 30-gauge needle. (Fig. 31) Possible complications include hyphema, (Fig. 32 – 33) endophthalmitis, increase in IOP requiring surgical intervention, and bleb failure.

Nd:YAG thermal laser treatment of overfiltering and leaking blebs has been described, although the success rate is limited. It is best done under



Figure 30 Optic nerve swelling, hypotony maculopathy following over filtration.

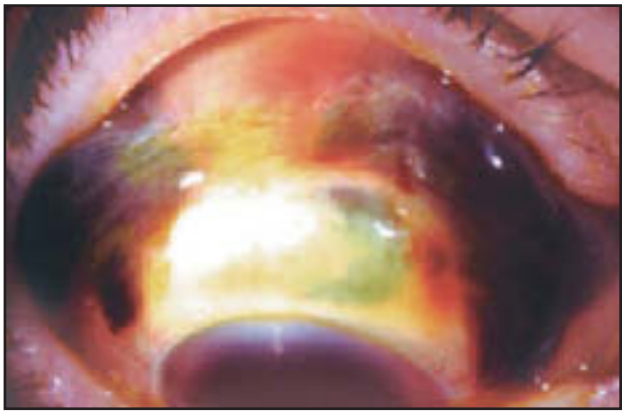


Figure 31 Autologous blood injection immediately postoperative. V.A. 20/80 pre-op, 4 mm Hg.

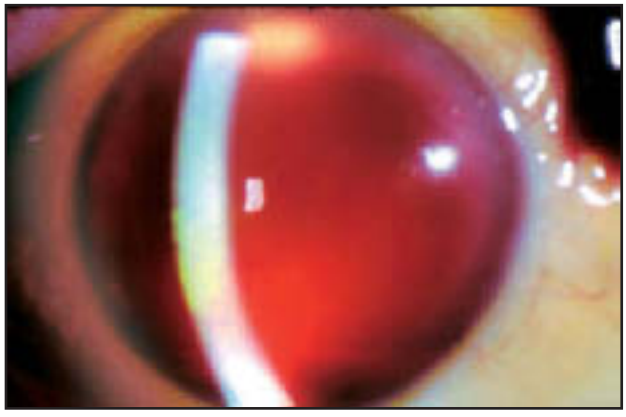


Figure 32 Hyphema immediately following autologous blood injection.

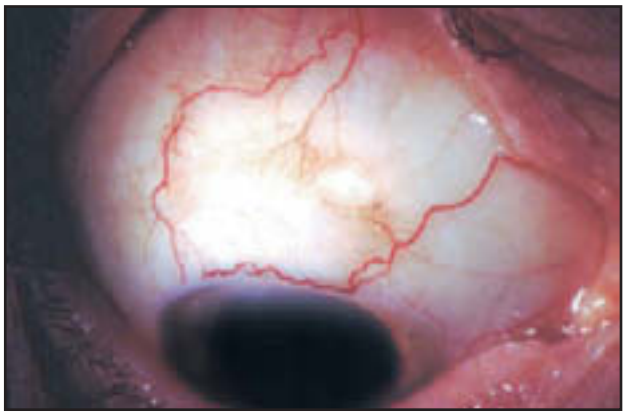


Figure 33 One month following autologous blood injection, IOP 10 mm Hg, V.A. 20/20.

regional anesthesia. For this procedure the continuous-wave mode is required. Energy levels range between 3.0 and 4.0 J, with the laser offset between 0.9 and 1.2 mm, and the aiming beam focused in the conjunctival epithelium. The goal is to induce whitening and wrinkling of the conjunctival epithelium. A grid pattern of 30 to 40 spots of laser placed over the entire bleb. Postoperatively oral aqueous suppressants and a compressive or "torpedo" (i.e., cotton plug placed directly over the bleb surface) patch are used during the first 48 hours. Cryotherapy, applying the probe to the lateral borders of the bleb and not directly over the filtering area, can be tried. Regional anesthesia is required. Before starting the freeze, firm pressure is applied with the cryoprobe to bring the bleb surface tissues into apposition with the underlying sclera. Several applications (2-5) of a temperature from -50 to -80ºC and a duration of application of 10-30 seconds are used. Waiting for the cryoprobe to thaw before moving it is essential to avoid tearing the bleb. Topical application of 0.25-1% silver nitrate or 50 % trichloracetic acid (TCA) to the bleb surface has been used by inducing a chemical conjunctival burn and consequent inflammation and stimulation of healing, although the success rate is very limited. Change in IOP occurs slowly in successful cases. After topical anesthesia, TCA or silver nitrate is sparingly administered directly to the conjunctival surface with the wooden end of a cotton-tip. After approximately 15-30 seconds the area is rinsed thoroughly. Corneal exposure must be avoided.

Finally, surgical revision for overfiltering blebs may be needed. (Fig. 34) Resuturing the scleral flap and scleral patch grafting (or patching with tutoplast – Fig. 4 – Editor) (when resuturing is not possible) have been successfully used in cases with hypotony maculopathy associated with overfiltering filtering bleb. Alternatively, mattress sutures anchored behind the bleb in episclera and anteriorly in the cornea can be used to compress the bleb. Cataract surgery in eyes with some lens opacities, without using postoperative steroids may improve hypotony.

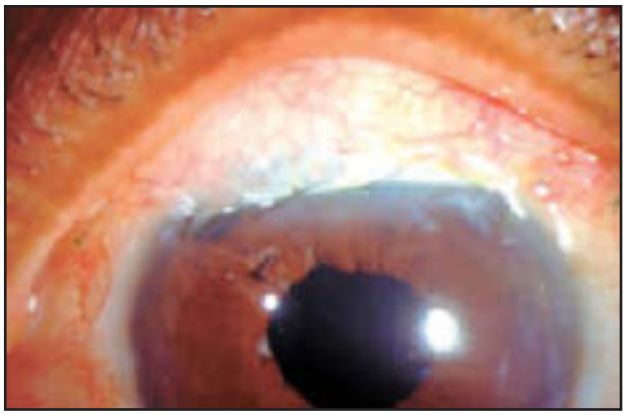


Figure 34 Surgical revision for overfiltering bleb, 3 Days post-op. IOP pre-op 2 mm Hg, post-op 14 mm Hg.

B. Hypotony due to Cyclodialysis Cleft

Chronic hypotony may occur after inadvertent creation of a cyclodialysis cleft. It can be associated with poor vision and hypotony maculopathy, and with no visible choroidal detachment. The anterior chamber can be formed or shallow, and there is no leak. Cyclodialisis clefts can be diagnosed by gonioscopy (Fig. 35) and by high-resolution ultrasound biomicroscopy. (ciliary body detachment posterior to the scleral spur may not be visible on gonioscopy and can be diagnosed by high resolution ultrasound biomicroscopy (Fig. 36) – **Editor**).

Treatment

Argon laser treatment can be used in an attempt to seal the cyclodialysis cleft. Laser settings are 100-200 mm spot sizes, 1-2 W power, and 0.1 sec duration. Regional anesthesia is usually required. The entire available scleral surface, starting in the depths of the cleft, and the choroid and ciliary body are treated. Following laser treatment the IOP should be monitored. Trans-scleral cryotherapy can be also tried.

If laser or cryotherapy is not effective, the ciliary body can be sutured directly to the sclera. A thick scleral flap extending 4 mm posteriorly is raised at the limbus overlying the detached ciliary body. Air or viscoelastic is injected into the anterior chamber. The remaining sclera is incised 1 mm posterior to the scleral spur. At this point, the cyclodialysis cleft is directly visualized. Then, interrupted 10/0 nylon sutures are passed from the anterior lip of sclera, then through the underlying ciliary body, avoiding the iris root, and again back through the posterior scleral lip. The superficial scleral flap is sutured back into place. Postoperative treatment include cycloplegics and, if necessary, aqueous suppressants.



Figure 35 Inadvertent cyclodialysis cleft following cataract surgery causing hypotony, IOP of 4 mm Hg.

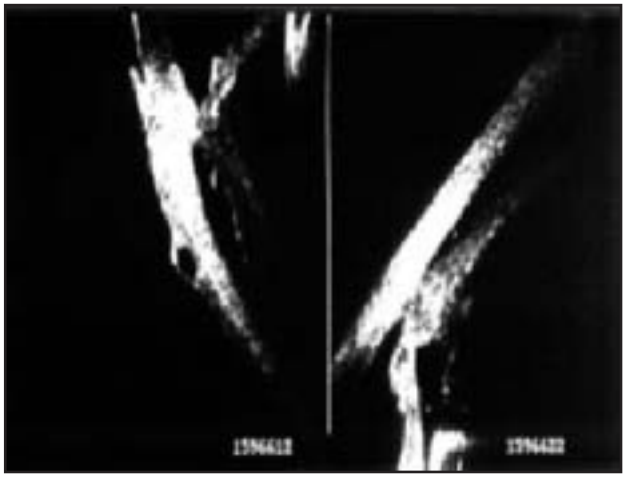


Figure 36 (Editor) (Ciliary body detachment posterior to the scleral spur demonstrated by high resolution ultrasound biomicroscopy (UBM). UBM performed by Dr. Jackson Coleman Editor)

C. Late Bleb Leak

Late bleb leaks can occur months or years after filtration surgery. Leaks are more likely to occur in avascular, thin blebs, which are seen more frequently when antimetabolites are used. Leakage of the filtering bleb can be associated with hypotony, shallow-flat anterior chamber and choroidal detachment, and may increase the chances for bleb infection and subsequent endophthalmitis. (Fig. 37)

The need and urgency of the management of bleb leaks depend on several factors. Some cases with history of previous bleb-related infections, shallow-flat anterior chamber, or reduced vision should be always treated. However, if there are no complications, such as in late leaks with formed blebs, normal intraocular pressure, good central vision and without previous episodes of bleb-related infection, the leak may not require therapy. Observation is possible to allow spontaneous closure of the leak. Pharmacological medical treatment with agents that decrease aqueous secretion (topical betablockers and/or CAI) and discontinuation of topical steroids, with or without patching, may help the spontaneous closure of these defects by reducing flow of aqueous through the fistula. Prophylactic broad spectrum antibiotic coverage, alternating different antibiotics, may be used. Patient education regarding symptoms of bleb-related ocular infection is crucial for prompt diagnosis and management.

Therapeutic modalities to treat late leaking blebs include pressure patching and bandage contact lens (see above), injection of autologous blood (see above), thermal Nd:YAG laser (see above), and surgical revision. When surgical revision is required, it is important to attempt to save the established initial filtration site. Due to the friable nature of the conjunctiva in long-established filtering blebs, it is often impossible to close the defect directly with sutures and, therefore, healthy conjunctival tissue is needed. First, the ischemic and thin-walled bleb tissue is denuded of conjunctival epithelium with mild cauterization to allow long-term adherence of the grafted conjunctiva. Fresh conjunctiva adjacent to the bleb is then mobilized to cover the previous filtration site by rotational, sliding or free conjunctival grafts. The conjunctiva is sutured over the previously abraded peripheral cornea with 10-0 nylon providing a watertight seal. Alternatively, radial compressing (delimiting) mattress sutures can be placed over the conjunctival surface, anchored behind the bleb in episclera and anteriorly in the cornea to isolate a leak from the remaining bleb and aid healing. Amniotic membrane can be used as an alternative substrate. With these methods bleb function can be usually preserved.

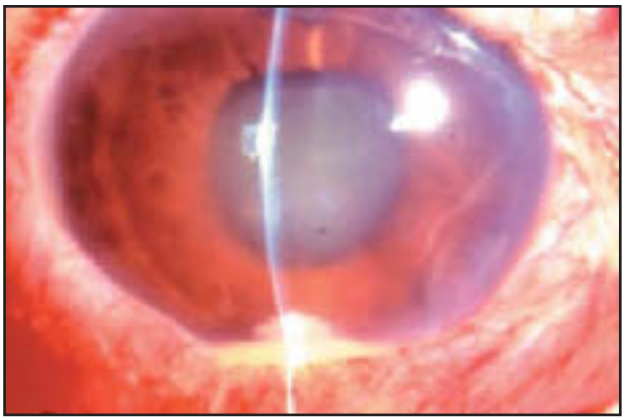


Figure 37 Endophthalmitis following a trabeculectomy. V.A. decreased to hand motion over a 24-hour period.

D. Bleb-Related Ocular Infection

Ocular infections related to filtration procedures can occur months to years after the initial surgery. Inferior filtering blebs, thin, localized and avascular blebs (more commonly seen after using antifibrotic agents) and leaks increase the probability of bleb-related ocular infection.

Bleb-related ocular infections can affect three compartments: the subconjunctival space (Stage I), the anterior segment (Stage II), and the vitreous cavity (Stage III). Usually the spread of infection proceeds in that order. Because the fluid within the bleb is continuous with the anterior chamber an infection of the bleb affecting the subconjunctival space ("blebitis") has a very real potential to rapidly spread posteriorly. The bacteria that cause bleb-related endophthalmitis almost certainly arise from the ocular flora. The most commonly involved organisms include Streptococcus species, H. influenza and Staphylococcus species.

Patients with bleb-related ocular infection usually present with ocular pain, blurred vision, tearing, redness and discharge. Examination reveals conjunctival and ciliary injection, most intense around the bleb edge, and purulent discharge. There may be periorbital chemosis. In Stage II and III anterior chamber reaction is noted, including frequently keratic precipitates, corneal edema and, in some cases, hypopyon. (Fig. 37) The bleb typically has a milky-white appearance with loss of clarity. A positive Seidel's test is common, and some patients may have a substantial leak, hypotony, and even flat anterior chamber. Alternatively, an increased IOP is possible due to internal closure of sclerostomy site with purulence and debris.

Vitreous reaction is not evident in early stages (Stage I and II) but, untreated, the infection spreads to the posterior segment (Stage III). If the media is not clear (e.g., dense cataract), B-mode ultrasonography can be helpful to detect involvement of the retrolental area.

The general principles that guide the management of ocular infections apply to this condition. It is important to identify the organism responsible. A conjunctival sample is routinely collected, stained and cultured. However, conjunctival culture in the etiologic diagnosis of bleb-related endophthalmitis has very little value. A vitreous sample should be obtained in stage III.

In stage I (blebitis without anterior chamber reaction) frequent topical application of a commercially available broad-spectrum antibiotic can be used, with very close supervision. Steroids can be considered to reduce the intense inflammation and preserve bleb integrity when the infection appears to be controlled. In stage II, (the anterior segment but not the posterior segment is involved), treatment with fortified topical antibiotics around the clock is advisable. Topical fortified cefazoline or vancomycin (25 mg/ml) associated with fortified tobramycin

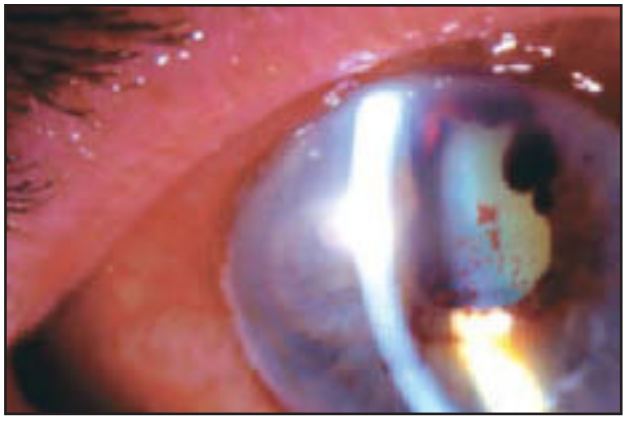


Figure 38 Cataract progression following a trabeculectomy complicated by hemorrhage into the anterior chamber.

(14 mg/ml), or amikacin (50 mg/ml) are likely to be effective against most gram-positive and gram-negative microorganisms. Additional systemic antibiotics can be used. In stage III (bleb-related endophthalmitis) intravitreal antibiotics are required, administered either through a pars plana injection at the time of sampling or associated with a vitrectomy. We are currently using 1 mg of vancomycin (10 mg/ml) and 400 mgr. of amikacin (5 mg/ml). Systemic antibiotics can be used. However, the Endophthalmitis Vitrectomy Study did not show any benefits of using systemic antibiotics in patients with endophthamitis after cataract surgery.

After resolution of the infection the function of the filtration bleb may be impaired. Other possible complications include corneal edema, cataract, vitreo-retinal traction and retinal toxicity from the bacteria's toxins or the antibiotics. The visual outcome is usually good in cases with anterior segment involvement and poor when the vitreous is involved, especially with virulent bacteria such as Streptococci, coagulase-positive Staphylococci, and gram-negative organisms.

Prevention of bleb-related ocular infection is important. Some ophthalmologists use long-term topical antibiotics after filtration procedures, although the efficacy of this regimen has been questioned. It seems reasonable to use long-term antibiotics in some cases of leaking blebs, inferior blebs, or recurrent bleb-related infections. Conjunctivitis and blepharitis should be treated promptly, and soft contact lens wear should be avoided. Patient education about early symptoms of infection is currently the most important approach to minimize the chances of severe visual loss.

E. Cataract Formation Following Filtration Surgery

Cataract formation and progression of pre-existing cataract can occur after filtration procedures. Lens opacification is the main cause of early visual loss after filtration surgery. The reported incidence varies from 2% to 53%. For example, in the Normal Tension Glaucoma Study, after 5 years of follow-up the incidence of cataract was 14% in the control group and 38% in the treated group, with the highest incidence in those whose treatment included filtration surgery.

Intraoperative lenticular trauma is possible, and can be recognized shortly after surgery. Intraoperative or postoperative flat anterior chamber with lens-corneal touch rapidly precipitates cataract formation. Other probable risk factors include age, presence of exfoliation, use of air to reform the anterior chamber, profound hypotony, use of miotics, topical steroids and inflammation.

Cataract extraction can be associated with a partial impairment of the function of the filtering bleb. Phacoemulsification of the lens with a corneal incision is the preferred method. Postoperative subconjunctival injections of 5-FU can be considered. If the control of IOP is sub-optimal, a combined cataract extraction and filtration procedure may be a preferred choice.

Chapter 32
SUPRACHOROIDAL HEMORRHAGE FOLLOWING GLAUCOMA FILTERING PROCEDURES

Lihteh Wu, M.D.

Suprachoroidal hemorrhage is a rare but catastrophic complication of intraocular surgery or ocular trauma. A sudden onset of hypotony plays a major role in this condition by causing a ciliochoroidal effusion. This effusion is thought to rupture the short or long posterior ciliary artery and its tributaries allowing blood to accumulate in the suprachoroidal space. A separation of the uvea from the sclera follows except at the ampullae of the vortex veins where the sclero-choroidal attachments are very firm. This gives rise to the typical dome shaped elevations of the fundus. Given the prominent role played by the sudden onset of hypotony in this condition, glaucoma filtering procedures are particularly prone to this complication.

Suprachoroidal hemorrhage may develop intraoperatively (expulsive) or post-operatively (delayed). Expulsion of the intraocular contents through the surgical wound usually occurs intraoperatively during a massive suprachoroidal hemorrhage. A delayed or post-operative suprachoroidal hemorrhage occurs in a closed system making expulsion of intraocular contents very rare. The incidence of expulsive suprachoroidal hemorrhage and delayed onset suprachoroidal hemorrhage following glaucoma filtering procedures has been reported to be 0.15% and 1.6% to 2% respectively.

Clinical Characteristics

An acute intraoperative suprachoroidal hemorrhage is characterized by loss of the red reflex, a sudden rise of intraocular pressure with hardening of the globe. The depth of the anterior chamber is lost as the intraocular contents (lens, vitreous, retina) prolapse forward. These may become incarcerated in the surgical wound.

Delayed-onset suprachoroidal hemorrhage usually presents with sudden pain that may awaken the patient from sleep, nausea, vomiting, diaphoresis and visual loss. The anterior chamber is usually flat. The iris and lens are displaced forward. The intraocular pressure may be low, normal or high. The funduscopic picture may range from a limited dome shaped elevation of the peripheral fundus that shallowly elevates the choroid and retina in one or more quadrants to an extensive form that fills the vitreous cavity causing apposition of the retina known as kissing choroidals. Retinal detachment and vitreous hemorrhage may be present (Fig. 1).

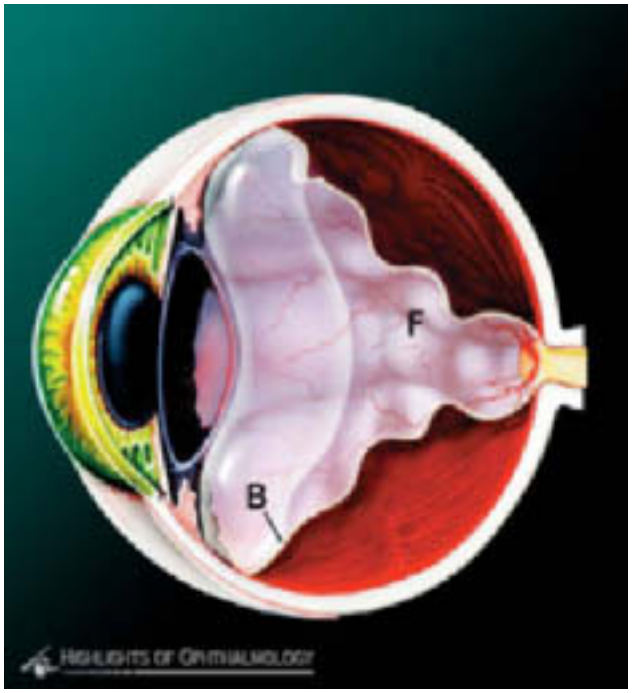


Fig. 1: Retinal Detachment following Suprachoroidal Hemorrhage

A postoperative suprachoroidal hemorrhage may occur even in a closed system technique resulting in expulsion of the intraocular contents. Ophthalmoscope examination may reveal a dome shaped elevation of the peripheral fundus (B) pushing up the choroid and retina in one or more quadrants. Retinal detachment (F) and vitreous hemorrhage may be present.

Risk Factors

Advanced age, glaucoma, increased axial length, aphakia or pseudophakia, sudden onset of ocular hypotony, systemic hypertension, Valsalva maneuvers and pre-operative ocular hypertension are all risk factors that have been identified in the development of a suprachoroidal hemorrhage.

Ultrasonographic Findings

Ophthalmic ultrasound is an useful adjunct in the diagnosis and management of suprachoroidal hemorrhage. Frequently the presence of opaque media does not allow a view of the fundus precluding a clinical diagnosis. Ultrasound permits identification of the elevated and detached choroid, blood in the suprachoroidal space, retinal detachment, vitreous hemorrhage and the progression of clot lysis. The optimal time for drainage depends on the liquefaction of the clot. Serial ultrasonographic examination is invaluable in determining the extent of clot liquefaction.

Typical B scan ultrasonographic findings include a smooth, dome shaped or flat membrane that does not move on dynamic testing (Fig. 2). The A-scan demonstrates a steeply rising double-peaked wide spike which is characteristic of a choroidal detachment. The lower reflective spikes in the suprachoroidal space represent blood.

The echographic appearance of the suprachoroidal space varies according to the state of liquefaction of the blood. When the suprachoroidal hemorrhage is composed of fresh clots, a highly reflective solid appearing mass with irregular internal structure and shape is imaged. With time, the clots decrease in size and its structure becomes more homogeneous. A lower and more regular internal reflectivity is seen echographically. If the clot has undergone significant lysis the gain may need to be

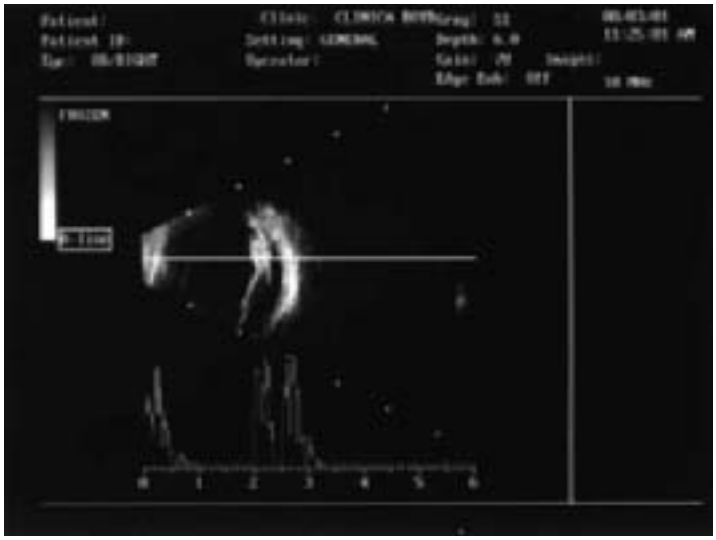


Fig. 2: B-Scan Ultrasonic Suprachoroidal Detachment

The typical B scan ultrasonic study usually include a smooth, dome shaped or flat membrane that does not move on dynamic testing. This membrane image in some instances elevates to an extensive form that fills the vitreous cavity causing apposition of the retina known as kissing choroidals (Courtesy of Samuel Boyd, M.D.).

turned up in order to detect the suprachoroidal blood. As the clot liquefies, the free blood can be seen moving freely in the suprachoroidal space during dynamic testing. Complete liquefaction of the clot is noted when the suprachoroidal space is seen to be filled with diffuse low-reflective mobile opacities. The mean clot lysis time may vary from 7 to 14 days.

Management

Recognition of an intraoperative expulsive suprachoroidal hemorrhage is of utmost importance. The first step is to immediately suture close all the incisions or to manually press on the incisions if these can't be sutured closed fast enough. The intraocular pressure rises as a result of these maneuvers and the bleeding vessel is tamponaded in this manner. Once the bleeding is controlled the expelled intraocular contents should be reposited back into the eye. The anterior chamber should be reformed with either BSS or air. This can prevent vitreous incarceration in the wound which is a risk factor in the development of a subsequent retinal detachment. The lid speculum should be removed to decrease direct pressure on the eye. Intravenous hyperosmotic agents and lowering of the systolic blood pressure have also been recommended. For many years posterior drainage sclerotomies were recommended in these situations. However, it is currently recognized that the blood in the suprachoroidal space clots very

quickly so by the time a posterior sclerotomy is made, drainage of the hemorrhage is virtually impossible. Furthermore, in a rabbit model of suprachoroidal hemorrhage, Lakhanpal found that immediate sclerotomy not only did not have a beneficial effect but was also detrimental since creation of the drainage sclerotomies resulted in expansion of the suprachoroidal hemorrhage and extension into the retina and vitreous cavity. The majority of the eyes that undergo primary drainage usually have to have a secondary drainage procedure. (In the Editor's experience, immediate posterior sclerotomy and drainage has been very helpful and most patients have not required a secondary drainage procedure – **Editor**) (Fig. 3).

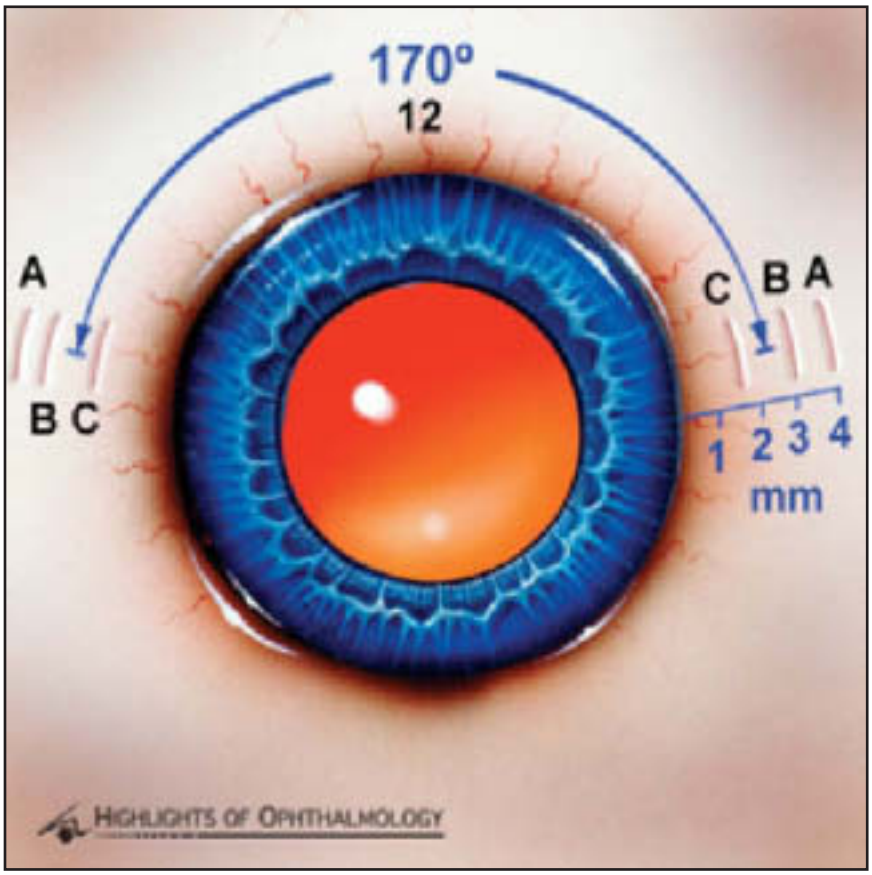
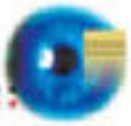


Fig. 3. : Placement of Posterior Sclerotomies for Drainage of Suprachoroidal Hemorrhage

Posterior Sclerotomies may be placed 3.5 – 4.0 mm posterior to the limbus (A) usually near the horizontal meridian (nasal or temporal side). In pseudophakic eyes, the sclerotomies can be safely placed at 3.0 mm posterior to the limbus (B). In retinal complicated cases with anterior PVR the approach may be at 1.5 – 2.0 mm posterior to the limbus (C).



The management of eyes with delayed-onset suprachoroidal hemorrhage is somewhat controversial in terms of deciding if and when surgical drainage should be recommended. In the past, early drainage was recommended. The problem with early drainage is the inability to drain when the blood is still clotted. Therefore most experts advise serial ultrasonographic examination to assess for blood liquefaction prior to attempting surgical drainage. Others have proposed the injection of 50 µg of t-PA into the suprachoroidal space 24 hours prior to surgery to facilitate clot liquefaction. It is unclear if eyes undergoing early drainage have a better outcome. Current indications for secondary drainage are eyes with nonresolving kissing choroidals, retinal detachment, persistent vitreous hemorrhage, iris or vitreous incarceration in the bleb, persistent pain or persistent flat chamber. However recent series from the Doheny Eye Institute and the Bascom Palmer Eye Institute have shown that not all eyes with appositional suprachoroidal hemorrhage need to be operated on.

Once the decision has been made to intervene surgically, the surgical goal should be to re-establish the normal anatomy of the eye. A conjunctival peritomy is performed to allow wide exposure. Traction sutures are used to loop the recti muscles. Fluid is then infused into the anterior chamber through the limbus. Sclerotomies are placed posterior to the ciliary body in the quadrants of highest elevation. Perfluorocarbon liquids are slowly injected into the vitreous cavity. As these settle posteriorly, liquefied blood is expressed through the sclerotomies. Notice that perfluorocarbon liquids are a useful adjunct as long as the clot has liquefied. In addition, if a retinal detachment is present, perfluorocarbon liquids may also be used to reattach the retina. Once the suprachoroidal blood has been drained, a standard 3 port pars plana vitrectomy is performed. Depending on the surgeon's choice and the pre-existing retinal pathology, the perfluorocarbon liquid is exchanged with silicone oil or a long-acting intraocular gas. A scleral buckle may or may not be indicated.

Visual Outcome

Even with current modern vitreoretinal techniques, the visual outcomes following drainage of a suprachoroidal hemorrhage are guarded. Most recent series report NLP in 22% to 30% of eyes despite drainage. Of the eyes that undergo surgical drainage, the severity of the suprachoroidal hemorrhage is a strong prognostic factor of visual function. Wirotsko and associates from the Medical College of Wisconsin have proposed a classification system that incorporates choroidal apposition and vitreous or retinal incarceration in the wound. According to this classification, eyes with only choroidal appositional (less severe) have a better outcome than eyes with either vitreous (severe) or retinal (more severe) incarceration.

Given the poor visual outcomes of this condition every effort should be made in the prevention of this complication. The preoperative intraocular pressure and the magnitude of the post-operative pressure reduction are important risk factors that are sometimes amenable to modification. (Controlled intraoperative intraocular pressure reduction is also helpful – **Editor**). It is recommended that eyes undergoing glaucoma filtering procedures should have preoperative lowering of intraocular pressure by using hyperosmotic agents if necessary and to use releasable sutures or argon suture lysis to minimize the acute intraocular pressure reduction.

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Chapter 33
ENDOPHTHALMITIS FOLLOWING GLAUCOMA SURGERY

Lihteh Wu, M.D.

Introduction

Infective endophthalmitis remains one of the most dreaded complications of any intraocular procedure and glaucoma filtering surgery is not the exception. As a matter of fact, the creation of a bleb during these procedures makes these eyes especially vulnerable to infection. Endophthalmitis is thought to occur in 0.1% of cases following cataract extraction. In contrast, 0.3% to 1.8% of eyes undergoing glaucoma filtering procedures will end up with infective endophthalmitis.

Clinical Signs and Symptoms

Most patients complain of an acute onset of ocular pain, blurred vision and redness months or even years after their glaucoma procedure. The pus filled bleb is often highlighted against the hyperemic conjunctiva giving the eye a "white on red" appearance. The conjunctiva over the bleb may have a leak or be intact. Other presenting signs may include anterior chamber inflammation, hypopyon, lid edema, chemosis, corneal edema, reduced red reflex, and an afferent pupillary defect. Vitritis is always present. The lack of pain or absence of hypopyon should not rule out the diagnosis of infective endophthalmitis. Although the Endophthalmitis Vitrectomy Study (EVS) did not enroll eyes that underwent glaucoma filtering procedures, it is noteworthy that pain was absent in 25% of patients, and hypopyon was absent in 14% of patients presenting with infective endophthalmitis. Therefore the hallmark sign of bacterial endophthalmitis is unexplained inflammation of the vitreous cavity.

Ciulla and colleagues proposed a useful classification scheme that differentiates between blebitis, early endophthalmitis and late endophthalmitis. The term blebitis was introduced by Brown and associates to denote infection confined to the bleb without involvement of the vitreous cavity. The importance of recognizing this entity is that it may be a harbinger of a more serious infection, yet if treated appropiately with topical fortified antibiotics, oral and subconjunctival antibiotics a relatively good visual outcome is achieved. Early or acute onset endophthalmitis is defined as that occurring 6 weeks or earlier following surgery and is presumably caused by intraoperative or perioperative introduction of

organisms into the eye. In their study, Staphylococcal species predominated in the early onset cases. Late or delayed onset endophthalmitis refers to those cases presenting after 6 weeks following surgery. These cases are thought to occur following transconjunctival penetration of bacteria into the bleb with extension into the anterior chamber and vitreous cavity. In a classic paper, Mandelbaum and co-workers identified Streptococci and Haemophilus species as the typical pathogens isolated in these conditions. However, more recently a report from the New York Eye & Ear Infirmary have found an increasing number of eyes infected with Staphylococcal species.

Risk Factors

There are several bleb features that predispose the eye to endophthalmitis. The presence of a bleb in of itself constitutes a ticking time bomb. The intraocular milieu is separated from the outside world by only a thin layer of conjunctiva. The use of anti-fibrotic adjuntive agents such as 5-Fluorouracil and Mitomycin C often results in thin walled avascular cystic blebs that makes these eyes highly permeable to microorganisms. Colonization of the bleb and infiltration into the eye may ensue. An inferior location of the bleb appears to be dangerous. Some series from the Bascom Palmer Eye Institute, the New York Eye and Ear Infirmary and the University of Michigan at Ann Arbor have reported as high as 11.5% of cases developing endophthalmitis in eyes with inferior blebs. Previous bleb manipulation (ie needling, suture lysis and contact lens use) has also been implicated in an increased risk of infection. Bleb leaks may allow direct access of bacteria into the eye.

Lid abnormalities such as blepharitis, distichiasis and entropion may predispose to infection by chronic infection or irritation of the bleb. Chronic dacryocystitis from nasolacrimal duct obstruction may result in collection of purulent material in the cul de sac and expose the bleb to it. Minor ocular trauma may rupture the bleb and cause it to leak.

Diagnosis

The diagnosis of infective endophthalmitis must often be made on clinical grounds alone. Due to the rapid progression of the disease, the initial management cannot be dependent on microbiologic results. However subsequent modification and tailoring of therapy is possible once culture results are available. Culture techniques can take between 2 and 12 days to confirm the presence and identity of the pathogen. A significant number of cultures remain negative presumably because of the low bacterial load found in intraocular samples. Modern molecular biologic techniques may be an useful adjunct to the microbiological culture techniques to detect and identify bacteria in ocular samples. In a study from the United Kingdom, Okhravi and colleagues were able to demonstrate bacterial DNA using polymerase chain reaction (PCR) based technology in 100% of samples compared to 68% using traditional techniques. The drawback is that it can't provide antibiotic sensitivity testing.

The vitreous followed by the aqueous is the site from which microbial isolation is most rewarding. Aqueous and vitreous samples are obtained in the following manner. A 27 to 30 gauge needle is attached to a tuberculin syringe and inserted through the limbus. Approximately 0.1 mL of aqueous is

aspirated. A vitreous sample may be obtained via needle aspiration or by the vitreous cutter (Fig. 1). Currently it appears that both methods are equally effective and the risks of complications (ie retinal detachment or tears) is similar among both methods.

A vitreous needle tap consists of aspiration of liquid vitreous through the pars plana with a 22 gauge to 27 gauge needle. In eyes undergoing a vitrectomy, the aspiration line of the vitrector is hooked to a tuberculin syringe. Infusion to the eye is kept closed until

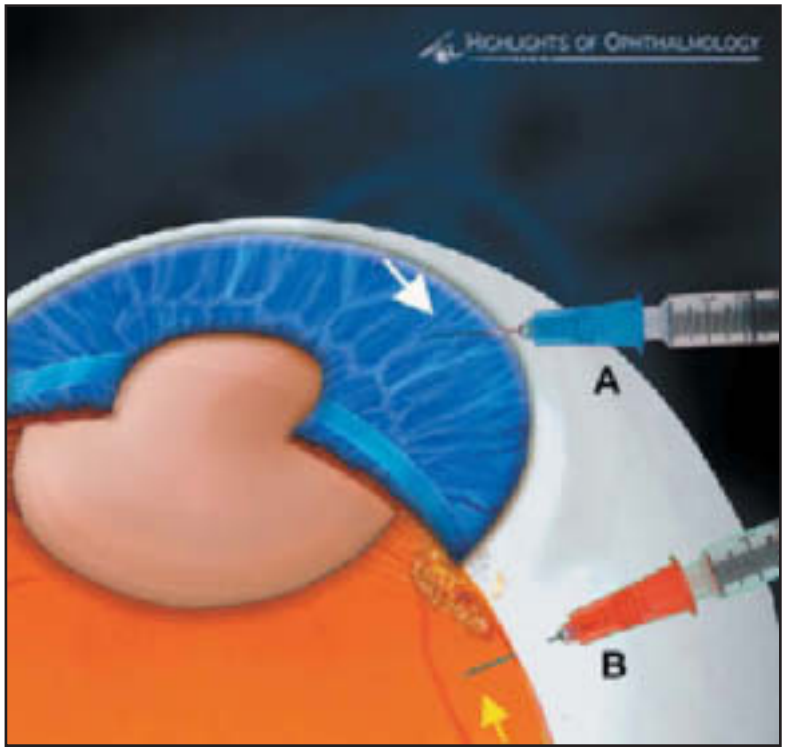


Fig. 1. Technique of Diagnosis with Aqueous Tap

A diagnostic tap may proceed from the anterior chamber (white arrow) or directly from the vitreous and consists of aspiration of contaminated fluid with a 22 - 27 gauge needle through the limbus (A) or through the pars plana (B). In the latter, always take good care to observe the extreme of the needle (yellow arrow) to avoid perforation of the retina.

the sample is withdrawn. The vitreous is cut and 0.1 to 0.3 mL of undiluted vitreous are manually aspirated into the syringe. The vitreous and aqueous samples are inoculated directly into the growth media. The vitrectomy cassette fluid is also sent for microbiologic analysis. Since the sample size is small and diluted it must be filtered and centrifuged in a sterile fashion prior to microbiologic analysis. Pieces of the filtered paper are then placed on the appropiate growth media.

The value of conjunctival and lid cultures is unknown. However, there is a poor correlation between intraocular (vitreous or aqueous) cultures and conjunctival / lid cultures. While a bleb aspirate is easily performed, it probably should not be done. Sampling of the bleb may lead to a leak given the friability of the tissue. Furthermore, the purulence may be too thick to allow a useful sample to be obtained.

Treatment

The mainstay of treatment for infective endophthalmitis remains the injection of broad spectrum intravitreal antibiotics. In very severe cases where the visual acuity on presentation is NLP, primary evisceration has been performed. Absolute care must be given in order to inject the correct concentration of antibiotic. Over-concentrated solutions have the potential of retinal toxicity and underconcentration of antibiotic will not kill the bacteria. This is particularly true for the aminoglycosides which can cause macular infarction when given in toxic doses.

Vancomycin is the agent of choice against Gram positive organisms. The recommended intravitreal dose is 1 mg in 0.1 mL of preservative free sterile water. This is prepared in the following manner. Ten mL of sterile water are added to a 500 mg vial of vancomycin powder. One ml of this solution is drawn into a 5 mL syringe. Four mL of sterile water are added into the syringe. This is mixed by drawing a small air bubble into the syringe and tilting it back and forth. It is recommended that in all these dilutions, a new needle is inserted into each new syringe. Slowly inject 0.1 ml of this solution into the midvitreous cavity with a 0.5 inch 30 gauge needle passed through pars plana (usually through closed sclerotomy) to the hilt and aimed at the middle of the eye. The recommended subconjunctival dose is 25 mg. 0.5 mL of the reconstituted solution (vancomycin 500 mg powder and 10 mL sterile water) is injected subconjuntivally.

Ceftazidime is the agent of choice against Gram negative organisms. To obtain the recommended intravitreal dose of 2.25 mg in 0.1 mL of preservative free sterile water, the following dilutions are performed. Ten mL of sterile water are added to a 1 gram vial of ceftazidime powder. 2.25 mL from the reconstituted vial are withdraw into a 10 ml syringe. 7.75 mL of sterile water without preservative are added and mixed to bring the volume in the syringe to 10 mL. 0.1 mL of this solution is injected in the midvitreous cavity. The recommended subconjunctival dose is 100 mg. One gram of ceftazidime in powder form is solubilized with 4.4 mL of sterile water. 0.5 mL of this solution is injected subconjunctivally.

If the patient is allergic to penicillin, amikacin is substituted for ceftazidime intravitreally and gentamicin for ceftazidime subconjunctivally. The recommended intravitreal dose of amikacin is 400 µg in 0.1 mL. A vial containing 500 mg in 2 mL of amikacin is obtained. One mL of this solution is drawn into a 10 mL syringe. Nine mL of sterile water without preservative are added and mixed into the syringe. The above solution is discarded until only 1.6 mL are left in the syringe. 8.4 mL of sterile water without preservative are added and mixed to bring the volume in the syringe to 10 mL. 0.1 mL of this solution is injected into the vitreous cavity. The recommended subconjunctival dose of gentamicin is 20 mg. Thus injection of 0.5 mL of undiluted gentamicin from the vial containing 80 mg/2 mL will provide this dose.

Intravenous, subconjunctival and topical antibiotics are commonly used but their value is unknown and should be considered adjunctive agents. The blood retinal barrier prevents the penetration of adequate levels of most antibiotics into the vitreous cavity when given intravenously. Oral quinolones such as levofloxacin (500 mg po bid) or ciprofloxacin (500 mg po bid) represent the exception and have a good intravitreal penetration. Therefore their use is not unreasonable.

Given the unique characteristics of infective endophthalmitis following glaucoma filtering

surgery, extrapolation from the Endophthalmitis Vitrectomy Study is not appropiate. It is not known if a vitrectomy is needed in these cases. However, given the rapid progression and poor visual outcome of this disease, most surgeons will probably elect to proceed with a vitrectomy and intravitreal antibiotics if this can be performed in a timely fashion. If for some reason, a vitrectomy can't be performed soon enough a vitreous tap with injection of intravitreal antibiotics should be performed as soon as possible. The theoretical advantages of a vitrectomy include reducing the inflammatory and bacterial load; elimination of sequestered pockets of infection; and increasing fluid circulation within the vitreous cavity allowing a better diffusion of antibiotics and enhancing the natural defense mechanisms of the eye. If a vitrectomy is considered, special care must be taken to avoid damaging the conjuntiva near the bleb as this is usually friable secondary to active infection. Due to poor visualization, vitrectomy in an infected eye is technically difficult. There is a high likelihood of iatrogenic damage to the retina if proper care is not taken. For this reason, a core vitrectomy rather than a complete vitrectomy is recommended (Fig. 2).

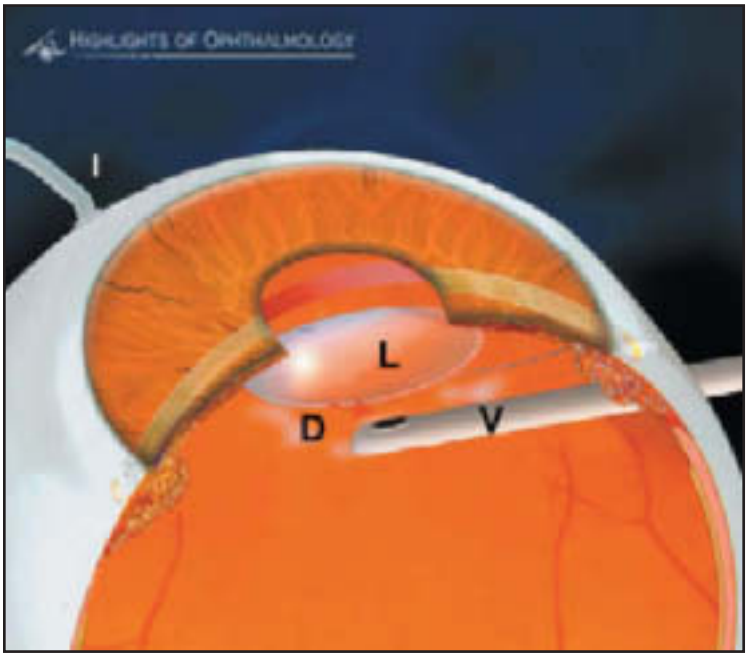


Fig. 2: Vitrectomy Procedure for the Management of Endophthalmitis

The main advantages of vitrectomy (V) in the management of endophthalmitis are focused in obtaining contaminated material for diagnosis, elimination of sequestered pockets of infection (D), reduction of inflammatory load and a better diffusion of intravitreal antibiotics. Intraocular lens (L), infusion canula (I).

The use of corticosteroids has been advocated to moderate the inflammatory response and improve visual outcome. Topical prednisolone acetate 1% is usually started the day following intravitreal antibiotic injection. Subconjunctival steroids have also been used but their role is unknown. The use of intravitreal corticosteroids is controversial and should be used on a case by case basis. The recommended dose is 0.4 mg of intravitreal dexamethasone. Some have advocated systemic steroids (60 mg to 100 mg prednisone) with a rapid taper over 5 to 14 days.

The treated eye commonly appears worse on the first post-treatment day and then improves subsequently. After 36 hours, culture results may be available. Worsening inflammation may warrant an additional injection of intravitreal antibiotics with or without vitrectomy.

If a small bleb leak is present it may be ignored in the acute setting. However, if the leak is severe, as evidenced by hypotony and a flat chamber, the leak must be repaired. One may use a scleral, dural or pericardial patch or mobilize the conjuntiva to cover the leak.

Outcomes

The virulence of the infecting organism is a strong clinical predictor of visual outcome. Patients in whom endophthalmitis develops after glaucoma filtering procedures do poorly, even with aggressive medical and surgical intervention. This probably reflects the bacterial virulence encountered in these cases. Final visual acuity has been reported to range from 20/25 to NLP in a recent report from the Bascom Palmer Eye Institute. In this same report, only 47% of eyes had a visual acuity better than 20/400. In comparison, the EVS reported that 74% of eyes achieved a final visual acuity of 20/100 or better.

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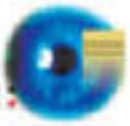
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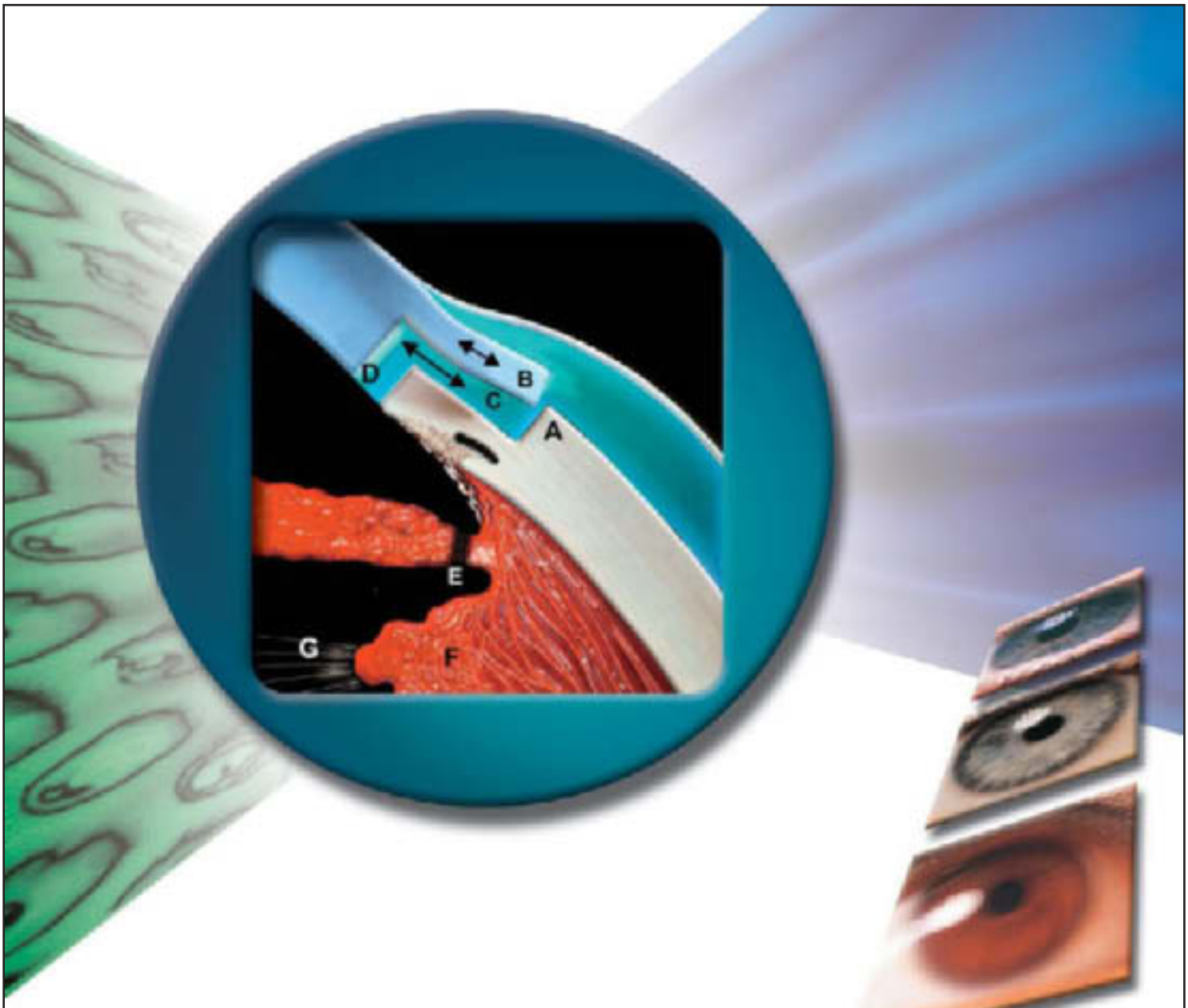
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SECTION VIII

Combined Cataract Surgery and Trabeculectomy



Chapter 34
PHACOTRABECULECTOMY
COMBINED CATARACT/TRABECULECTOMY SURGERY FOR GLAUCOMA

Rafael I. Barraquer, M.D.

The new developments in combined surgery for cataract and glaucoma can be summarized as the consequences of two current trends: minimization of the incision for cataract extraction and use of antimetabolites to enhance filtration. This short review will focus on the cataract-trabeculectomy operation. New alternative procedures such as endoscopic cyclophotocoagulation, laser sclerostomy, trabecular aspiration, visco-canalostomy, non-penetrating deep sclerectomy and filtration-enhancing implants lie beyond its scope.

Indications

The prior question on the indication of combined vs succesive surgery is a complex one, including medical, surgical, and logistic-economic factors. Although this has not yet been completely settled, a strong trend favors combined procedures- at least in our environment. Actually, long-term data from our institution indicate that, even since the intracapsular era, combined operations are as good as trabeculectomies alone for the control of glaucoma. In the presence of independent indications for glaucoma and cataract surgery even if the cataract is not far advanced, the advantages for the patient of a single combined procedure appear to outweigh the possibly slower visual recovery and the more intensive postoperative care.

Integrated vs Independent Access

During the planned extracapsular, large incision (nuclear expression) period, the main technical choice was between an "integrated" access - limbal (sclerocorneal) cataract incision as a lateral enlargement of the trabeculectomy incision under the flap - vs. an independent one - with a clear corneal incision for the cataract phase. Similarly to the dilemma between fornix (FBF) and limbus-based conjunctival flaps (LBF), this appeared to have little influence on the outcome and became a question of surgeon preference.

The advent of small incision cataract surgery - either ultrasound-assisted aspiration (phaoemulsification) through 3-4 mm or manual nuclear fragmentation and extraction through 5-6 mm - has strongly supported the case for an integrated access. Since the cataract can be extracted through the same small incision used for the trabeculectomy alone, an independent incision for each phase seems harder to justify. The ensuing term phacotrabeculectomy usually refers to the use of an ultrasound probe for the cataract extraction. It should be noted, however, that according to the actual etymology of the prefix "phaco"-(from the Greek for "lens"), the term "phacotrabeculectomy" could be applied to any cataract-trabeculectomy procedure - even intracapsular.

Several technical issues stem from or are modified by this new approach. Some are old, as the convenience of a FBF vs LBF, other more recent, as whether to use antimetabolites routinely. Some are specific of phacotrabeculectomy, such as making a scleral trapdoor vs. a tunnel incision, using foldable vs. rigid intraocular lenses (IOL), and whether the scleral sutures could-should be obviated. Rather than proposing a standard procedure, I will discuss the pros and cons of each of the alternatives.

Fornix vs. Limbus-Based Conjunctival Flap

The selection of the conjunctival flap, either fornix (FBF) or limbus-based (LBF), can be considered simply a question of surgeon preference (Fig. 1 A-B). Both types can be used with similar success and complication rates - except for a higher early Seidel (+) test with FBF, which is generally transient. A LBF flap makes visualization of the surgical field slightly more difficult and usually requires more suturing-either interrupted or running. It can also be difficult to dissect in cases of re-operation with increased risk of buttonholing. A FBF may result in slightly more anterior blebs, with a tendency to advance over the cornea - an undesirable effect in, e.g., the presence of a corneal graft-, while the posterior scar of a LBF might act as a barrier to filtration (Fig. 2 A-C).

The introduction of mitomycin initially favored the use of LBF to avoid the early - though transient - leakage problem of FBF (Fig. 3A-B). However, the disadvantage may be compensated by the more posterior opening of the filter in the case of a phacotrabeculectomy with tunnel incision, and because of its simplicity and better exposure give FBF a technical edge over LBF. In any case the suturing - at the limbal sides of a FBF - has to be meticulous in order to ensure a watertight closure (Fig. 4A-C).

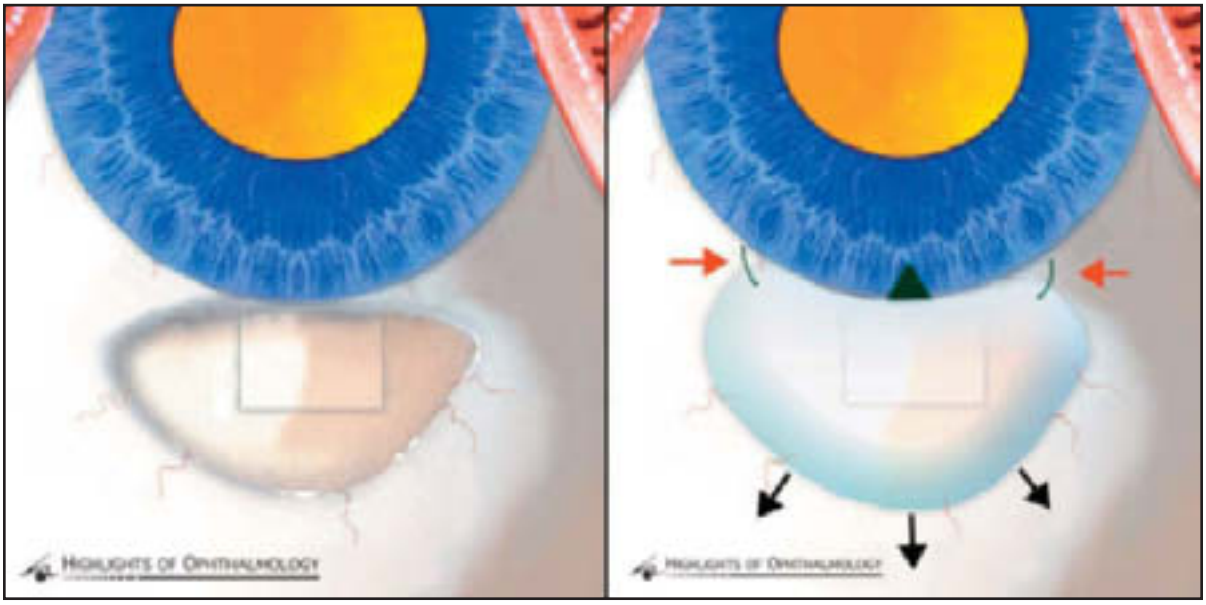


Fig. 1 A-B. Advantages of the Fornix Based Flap
The main advantages include a better surgical exposure **(A)** and an easier two-stitch closure **(B)**.

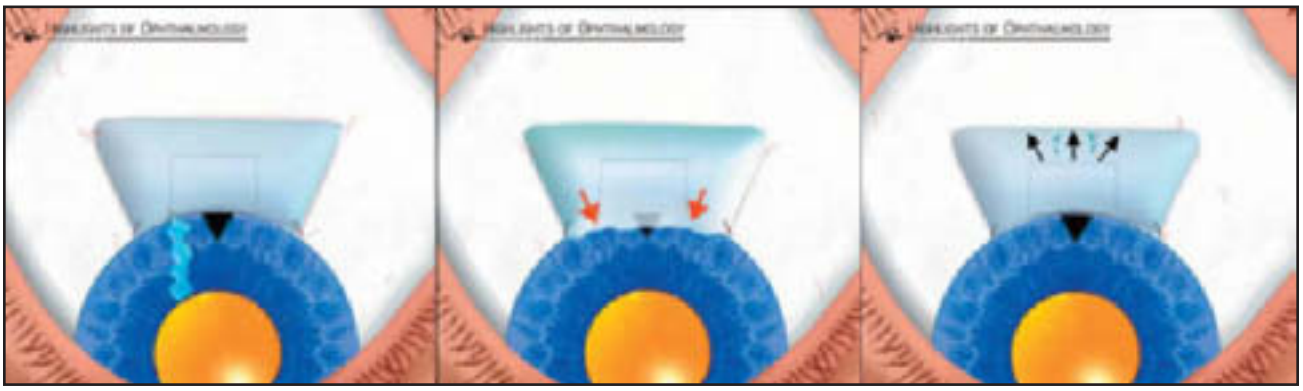


Fig. 2 A-C. Disadvantages of the Fornix Based Flap

Disadvantages may include early postoperative leaks (especially if antimetabolites are used) **(A)**, and a tendency to anterior displacement of the filtering bleb **(B)**. These disadvantages are minimized by the posterior and only fluid flow from the tunnel phacotrabeculectomy opening **(arrows-C)**.

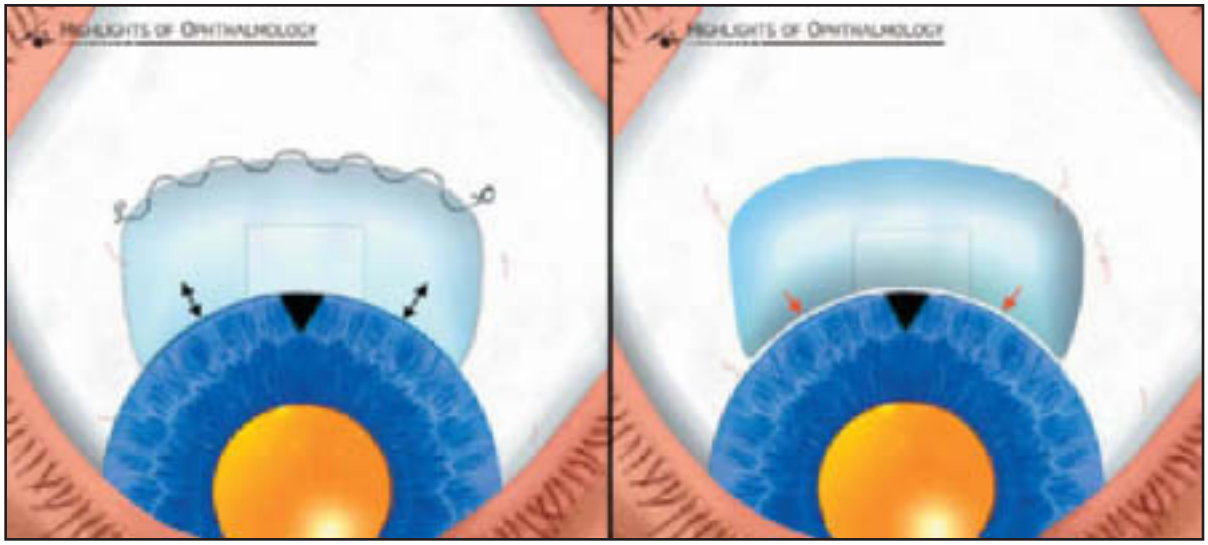


Fig. 3 A-B. Advantages of the Limbus Based Flap

These include the fact that if there is limbal leakage **(A)** it is not early thereby not resulting in defficient anterior chamber reformation. In addition the blebs tend to stay away from the cornea **(B)**.

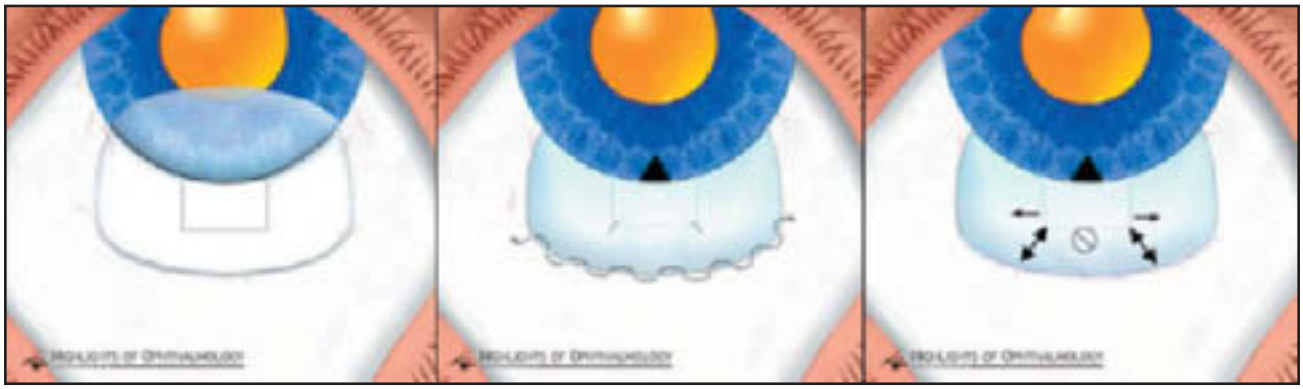


Fig. 4 A-C. Disadvantages of the Limbus Based Flap.
This three step illustration presents a poorer surgical exposure (the flap obstructs the view) **(A)**, requiring multiple single or running sutures **(B)**. The posterior scarring at the site of the flap suture may limit filtration and makes dissection difficult in case of reoperation (risk of buttonholing) **(C)**.

Use of Antimetabolites

The introduction of antimetabolites is acknowledged as one of the major advances in modern glaucoma surgery. However, the issue on their precise indications is still unsettled, particularly for primary cases because of a narrower risk-benefit ratio. At our institution routine use of low-dose mitomycin C in primary combined procedures was started at the time large incision extracaps was the rule. A definite improvement in the results was evident, with only a minor increase in complications. I believe the latter fact was the consequence of using low concentrations (0.2 mg-mL) and short exposures (2 minutes) in cases without known risk factors for failure. When any of these were present we extend the exposure to 5 minutes.

We have maintained this policy with the transition to phacotrabeculectomy. (**Editor's Note**: a Weck cell sponge is soaked in mitomycin and may be placed either on the intact conjunctiva (transconjunctiva) or under the conjunctiva on the intact sclera for the time and in the consideration indicated above. This is done before the scleral tunnel is dissected.)

Scleral Flap vs. Tunnel Incision

The use of a classical open-sided trapdoor or scleral flap to guard the actual trabeculectomy - irrespective of its size and shape, square, trapezoidal, triangular, round - vs. a tunnel incision is a main technical issue specific to phacotrabeculectomy, since both could be used in principle. The first choice represents the conservative approach, based on the proven efficacy of the classical technique, creates a better exposure and should allow for a more copious filtration, but means more surgery and commonly mandates suturing (Fig. 5A-B).

Sclerocorneal tunnel incisions are the result of the search for a self-sealing - ideally sutureless - incision in modern cataract surgery. This may appear paradoxical when applied to a glaucoma filtering procedure. However, the resection of the deep limbal tissues (trabeculectomy) at the inner entrance to the tunnel appears to negate its self-sealing quality and allows for a filtration. The fact that this is restricted to the only exit of the tunnel which is posterior to the limbus, may be considered an advantage in order to avoid over-filtration - especially towards

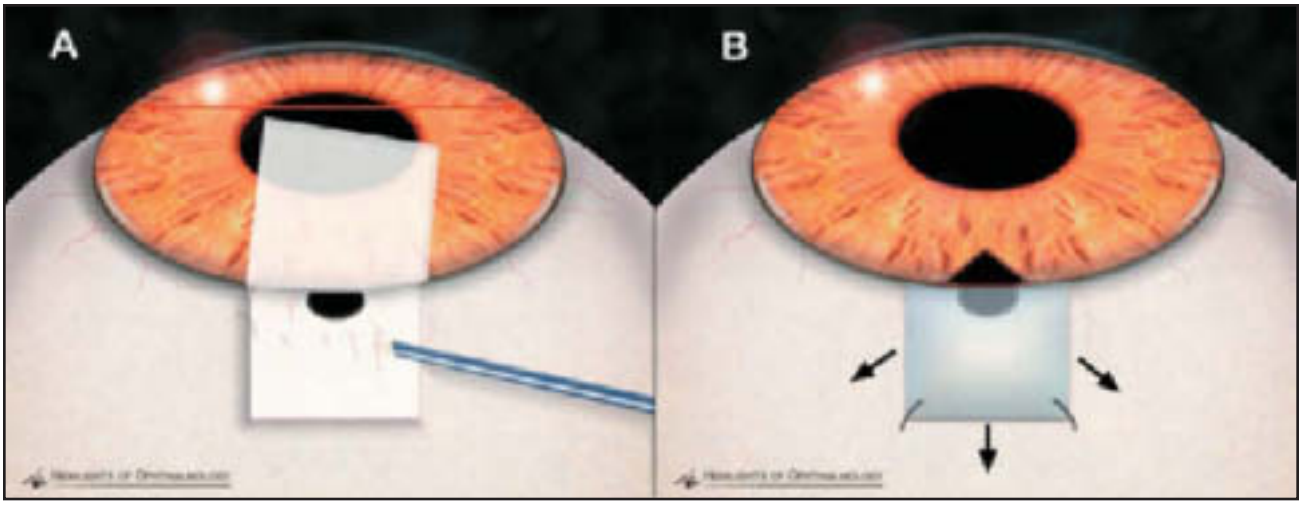


Fig. 5 A-B. Advantages and Disadvantages of the Scleral Flap vs Tunnel Incision

(A)The scleral flap approach offers a better exposure of the trabeculectomy site, easier to perform hemostasis and peripheral iridectomy. The trabecular resection does not require special instruments. **(B)** At the end of surgery the scleral flap requires suturing thereby inducing astigmatism. It may also lead to a more copious filtration (posterior and lateral-arrows).

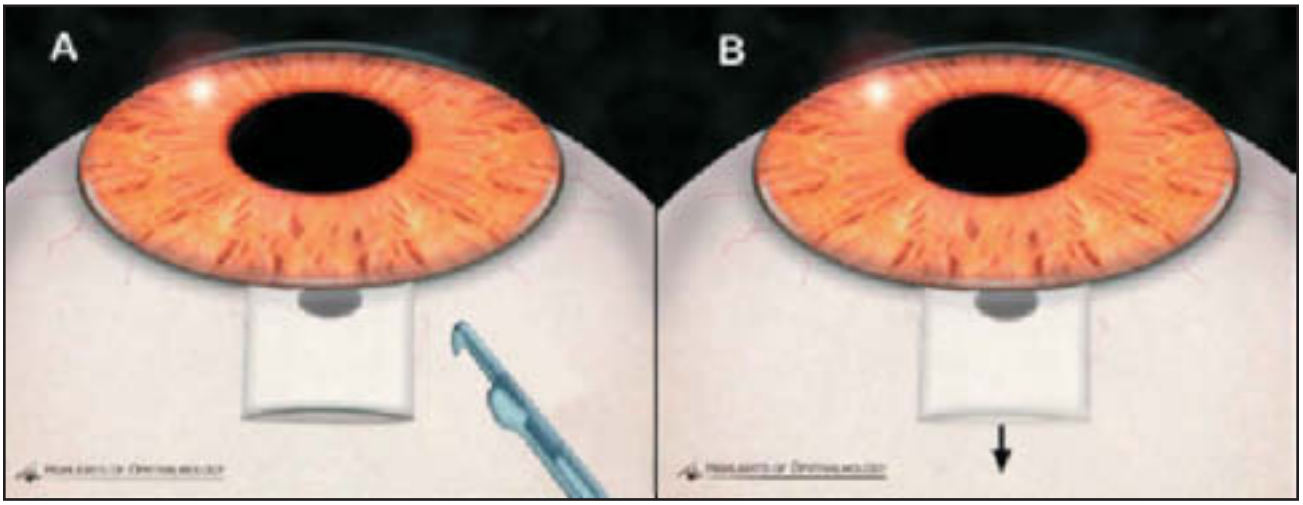


Fig. 6 A-B. Advantages and disadvantages of the Tunnel Incision vs the Scleral Flap

(A)Disadvantages include poor exposure of the trabeculectomy site. Hemostasis and iridectomy may be more difficult. This procedure requires a special punch. **(B)** At the end of surgery the incision may be left sutureless, minimizing induced astigmatism. The filtration is limited to the posterior direction (arrow).

the anterior (limbal) zone and creating leakage or overhanging blebs.

However, the exposure is poorer, requiring the use of a scleral punch specially designed for tunnels - such as the Luntz-Dodick or the Crozafon-De Laage - and makes more difficult some maneuvers such as the peripheral iridectomy or insuring hemostasis in case of a bleeder inside the tunnel (Fig. 6A-B). Nevertheless this appears to be the trend for phacotrabeculectomy, possibly due to its simplicity, the minimization of induced astigmatism, and the desirability of avoiding scleral sutures. (**Editor's Note**: When the tunnel scleral incision is used for phacotrabeculectomy, no radial incisions are made at the site of the scleral tunnel. This limits drainage through the scleral tunnel and prevents overdrainage; for this reason sutures are not mandatory.)

Foldable vs Rigid IOL

The advantages of small incision cataract surgery are ideally completed by the use of a foldable IOL. Consequently, it may appear that foldable implants are best suited for phacotrabeculectomy. However some favor the use of rigid-optic IOLs for plain cataract surgery - even with small incision extraction - and what is best for cataract alone may not necessarily be so for combined surgery.

One of the main advantages of reducing the incision to the size (under 4 mm) which requires the use of a foldable IOL, i.e., minimizing induced astigmatism - evident in the case of a clear corneal approach - becomes marginal in the case of a phacotrabeculectomy. A scleral tunnel wide enough for the implantation of a 5 to 5.5 mm rigid-optics IOL can be almost as anastigmatic.

The use of foldable IOLs in combined surgery may have disadvantages such as an increased risk of postoperative shallow or flat anterior chamber. The rarity of flat chambers - in our hands - with the use of the classic (rigid-optic, single-piece, C-loop) posterior chamber IOLs contrasted with our first impressions after we started performing phacotrabeculectomy with foldable IOLs. A cluster of adverse events can be the result of chance, however; little is known about how the different foldable materials and designs influence the stability of the irido-lenticulo-capsular plane relative to aqueous dynamics. This is a complex problem that possibly depends on multiple additional factors including the design of the tunnel-scleral flap, the size of the sclerectomy, the use of antimetabolites and the number and tension of the sutures. (**Editor's Note**: Foldable IOL's are used by most surgeons with good results for phacotrabeculectomy and for the advantage over the rigid optic IOL's that there is no need to enlarge the small incision. The smaller incision theoretically should have fewer postoperative complications.)

To Suture Or Not To Suture

A final but no less important issue posed by phacotrabeculectomy is the possibility to obviate all suturing. Until better tissue adhesives become available, sutures will be mandatory at least for the conjunctival flap - especially if antimetabolites are used. The need for sutures at the scleral flap-tunnel constitute a completely different matter, since their function is not to obtain a watertight closure but to limit the filtration and to allow for a certain filtration of the flow. Again, what may appear, as the ideal for cataract surgery - a sutureless procedure -, may not be the best for combined cataract-glaucoma. It is definitely possible to perform a functioning sutureless tunnel phacotrabeculectomy, but this is far from stating that this should be the preferred technique.

Renouncing the use of sutures implies that the actual filtration will depend on other factors that may be hard to control in a reproducible way. These include several features of the construction of the tunnel as its length, width, and shape of the posterior (external) opening, which will determine its tendency to gape. Multiple factors may be particularly variable or plainly uncontrollable: the distance between the tunnel entrance and the actual position of the "trabeculectomy" resection - not just the distance to the limbus, itself a fuzzy one, the thickness of the tunnel roof and the patient’s scleral rigidity; the response of

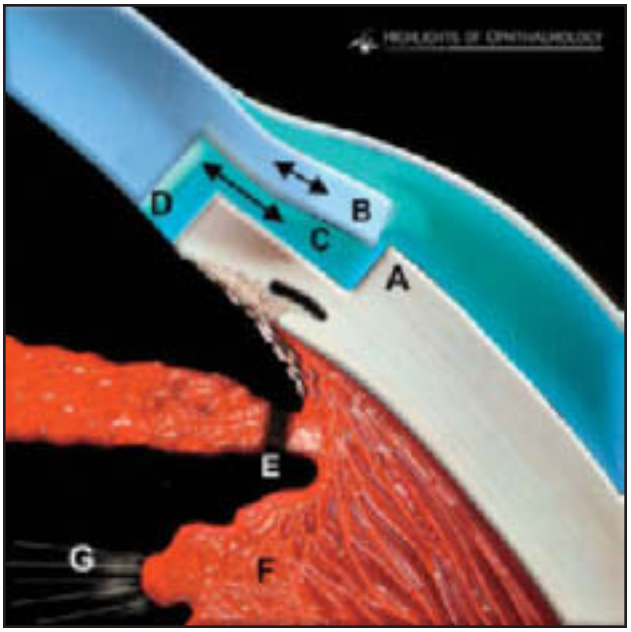
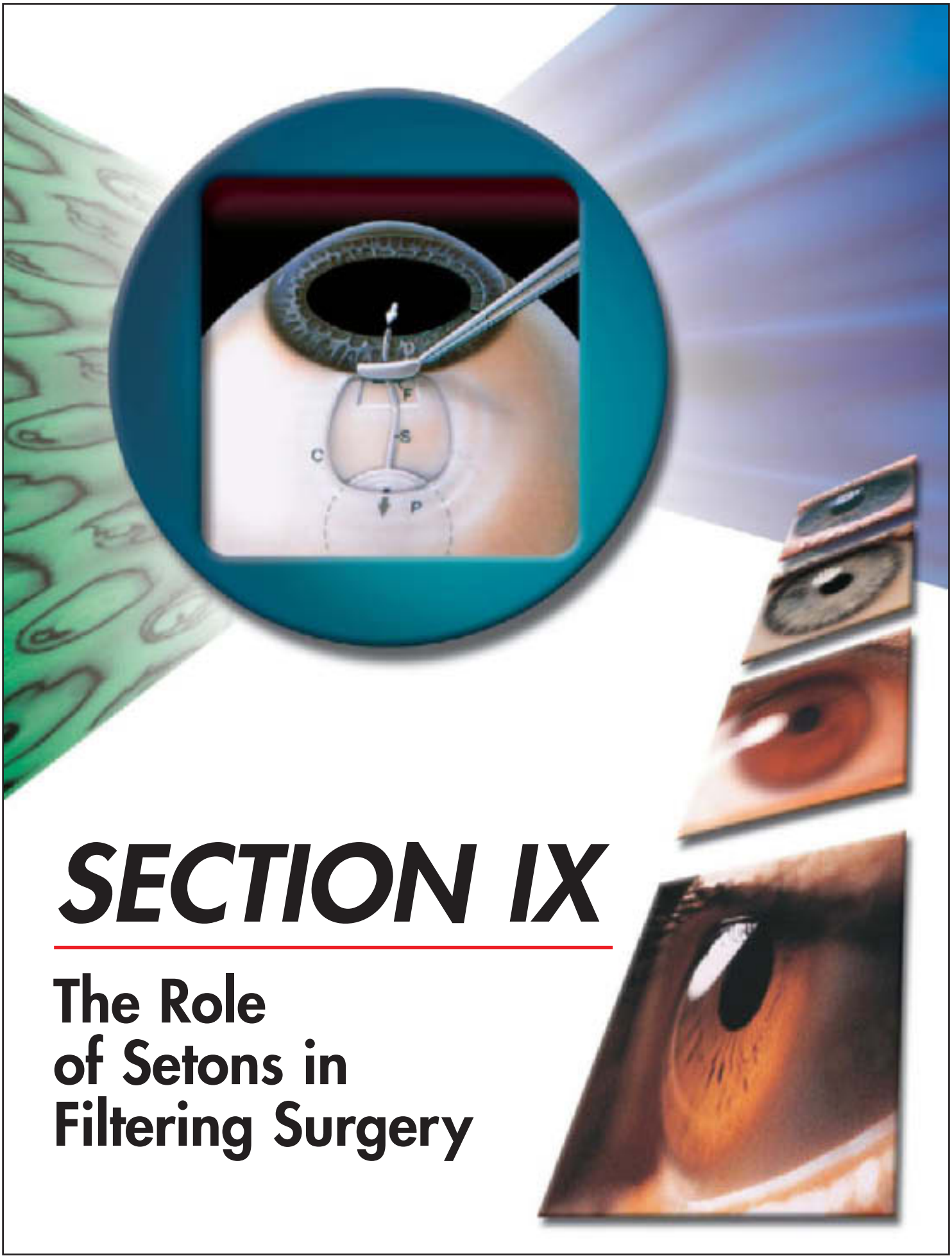


Fig. 7. Factors that may Influence Filtration in a Sutureless Scleral Tunnel Phacotrabeculectomy

These factors are usually related to **(A)** the posterior "external" opening of the tunnel: not only its width, but also its shape (linear, smile, frown, etc.). **(B)** Tunnel "roof": its thickness and patient´s scleral rigidity will influence the gaping of the posterior opening (A). **(C)** Tunnel length: Extends not only to the limbus, but to the actual position of the trabeculectomy (A to D). **(D)** Inner corneo-scleral resection (trabeculectomy). Its size may be less relevant than its position – not just relative to (A), but proximity to the ciliary body may favor postoperative inflammation and scarring leading to creation of an early cyclodyalisis. **(E)** Peripheral iridectomy. If insufficient or misplaced it may lead to synachiae and closure of the filtration. **(F)** Aqueous forming apparatus: early response to surgical trauma and possible toxicity of antimetabolites may contribute to postoperative hypotony. **(G)** Possible effects of zonular tension on ciliary body and trabecular area depending on design and placement of IOL. **(H)** Hemostasis. Any blood collection either from conjunctiva, Tenon´s scleral tunnel, iris root, etc. can compromise the functioning of the filtration and promote scarring.

the aqueous forming apparatus to surgical trauma, among others (Fig. 7). The influence of mitomycin on the early filtration rate and risk of overfiltration is not clear. In principle, its effects should not be apparent until the later processes of cellular proliferation and fibrosis take place. (**Editor's Note**: the author is correct to point out the multiple factors that may influence the drainage of aqueous in a scleral tunnel incision for phacotrabeculectomy. However, these variables cannot be measured and there is no direct evidence that this will affect the drainage whether sutures are used or not used. The procedure works well without sutures as explained in the previous editorial note.)

Leaving apart the benefit from becoming aware of the importance of these subtler factors on filtration, we still favor the placement of one or several sutures at the tunnel opening. In order to have the capability to titrate the effect of our surgery, it is preferable to combine a flap-tunnel designed for a generous filtration with limiting sutures that can be constructed as releasable or laser cut if necessary in the early postoperative period.



SECTION IX

The Role of Setons in Filtering Surgery

Chapter 35
INDICATIONS FOR IMPLANTATION - HOW SETONS FUNCTION

Benjamin F. Boyd, M.D., F.A.C.S.
Maurice Luntz, M.D., F.A.C.S.

Selecting the Procedure of Choice

Modern ophthalmic seton devices have shown encouraging results in many forms of refractory secondary glaucomas, including those in aphakic and pseudophakic eyes and those associated with epithelial downgrowth. Their use, however, is definitely decreased since the advent of filtration procedures combined with intraoperative and postoperative 5-FU or intraoperative mitomycin. The use of these antimetabolites have significantly increased the success of filtration procedures in high risk glaucomatous eyes (aphakic, pseudophakic, previous filtration failures and young patients).(1)

As a matter of fact, a conventional trabeculectomy procedure **with antimetabolites** generally seems to result in better intraocular pressure control levels than those obtained with a seton procedure, unless the conjunctiva is very much affected by scarring. There is no irrefutable evidence in the literature whether a seton is better than a filtering operation with antimetabolites.

The **main indication** for a Seton implant is when the intraocular pressure does not respond to medical therapy and the conjunctiva is **extensively scarred in all quadrants** from previous conventional filtration procedures that have failed.(2) In such a situation, another conventional filtration procedure even if combined with antimetabolites (5-FU or mitomycin) has limited chance to work. A seton is the operation of choice in neovascular glaucoma.(3) Some surgeons prefer to use a seton as their primary filtering operation rather than trabeculectomy but as an initial surgical procedure for medically uncontrolled glaucoma setons are not widely used. Setons have the advantage that, the base plate placed well posteriorly on the sclera produces a bleb posteriorly which is far less likely to be thin and substantially reduces the risk of endophthalmitis (See Figs. 1 and 2).

However, trabeculectomy with mitomycin is a better IOP lowering procedure. To evaluate these two treatments Parrish is conducting a clinical trial.



Fig. 1: Mechanism of Function of Setons in Avoiding Fibrosis of the Bleb

Figure 1 shows a section of the globe with the Seton in place. Aqueous in the anterior chamber (A-arrow) passes to the base plate (P-arrow) via the silicone tube (S). The implant has a biconcave shape with the inferior surface shaped to fit the sclera. Failure of the bleb (B) is avoided as the aqueous drains from the plate (P) post-equatorially. Blebs located post- equatorially are less likely to fibrose down than those located more anteriorly as seen in Fig. 2.



Figure 2: Comparison of Bleb Location Between Conventional Filtering Operation and Following Seton Implantation

Figure 2 shows a conventional filtering operation with fistula (F) and a filtering bleb (B) above a scleral flap covering a seton plate. The location of the bleb and seton anteriorly is more likely to fibrose down than setons with consequent filtering blebs located posteriorly, as shown in Fig. 1.

A difficult decision is to decide **when to use a seton** or shunt device vs a **cyclophotocoagulation or photoablative procedure (See chapter 42)**. The decision depends on the visual acuity of the eye involved, the condition of the visual fields, how much function is present in the fellow eye and the patient's general health status.

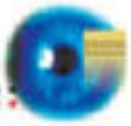
Long term visual results are better with the seton procedure which is another type of filtration operation. With the cyclophotoablative procedures, there is usually some visual loss and the long-term visual results are poorer. In addition, the incidence of sympathetic ophthalmia after Nd:YAG cyclotherapy although rare is higher than with other ocular procedures.

Therefore, if central visual acuity is still reasonably good, a seton procedure is preferable. On the other hand, if fixation has already been lost and all we can do for the patient is to preserve the remaining visual fields, which in most cases are severely affected, cyclophotocoagulation is the procedure of choice. The same applies to patients with neovascular glaucoma and those who are in poor health and do not have a favorable life expectancy. In these cases, cyclophotocoagulation is the procedure of choice because it is less traumatic than the more extensive seton surgery.

If the previously described equipment necessary to perform a laser cyclophotocoagulation is not available, cyclocryotherapy would then be used in its place, following the same indications.

Drainage Implant Surgery versus Limbal Trabeculectomy with Antimetabolites

Parrish is now seeking to determine the best treatment for eyes with glaucoma that have a worse than usual prognosis, such as after failed trabeculectomy or previous cataract surgery. He, **Dr. Steven Gedde** of the Bascom Palmer Eye Institute, and **Dr. Dale Heuer,** Chairman of Ophthalmology, Medical College of Wisconsin, have designed a clinical trial, the **TVT** (tube versus trabeculectomy) that will compare the safety and effectiveness of drainage implant surgery using a 350 mm Baerveldt implant (Pharmacia) to a standard limbal trabeculectomy with antimetabolites. Patients with poor prognosis are now being randomly assigned to one of these two surgical treatments at 13 clinical centers.



According to **Parrish** many ophthalmologists believe that the risk of late bleb or intraocular infections associated with drainage implants is substantially less than with trabeculectomy and mitomycin C. Intraocular pressures in the very high range, such as 30 - 40 mmHg, are less likely to be lowered immediately after drainage implant surgery than with a trabeculectomy with antimetabolite. The most efficient and ethical way to sort out the benefits and risks of these two treatments is to conduct a clinical trial. The study will determine which of these two techniques will provide the most effective and safest method of lowering intraocular pressure. Independent funding to support this trial is being provided by Pharmacia.

The two most used non-valvulated implants are the Molteno and the Baerveldt. The Molteno has had the longest follow-up. There are also valvulated implants (Krupin implant and Ahmed implant). (See chapters 34, 36, 37, 38)

Surgical Technique for Seton Implantation

The one mostly used has been the **Molteno** implant but the Ahmed valved implant and the Baerveldt are becoming the setons of choice. The Molteno implant consists of a silicone tube without a valve, which is placed into the anterior chamber and shunts aqueous to a polymethyl methacrylate plate sutured to the episclera near the equator (Figs. 1 and 2). The plate becomes encapsulated by fibrous tissue and forms a bleb producing an aqueous reservoir which is formed far posteriorly, near the equator where Tenon's tissue is thinner and less reactive than at the limbus. Overfiltration is common immediately post-surgery due to unrestricted flow of aqueous through the seton tube. The Molteno implant is like a plastic dome separating the conjunctiva from the sclera to maintain a subconjunctival reservoir into which the aqueous can flow. The surgical results have improved with the use of a double -plate Molteno implant.

Results vary with different authors. Most report from 63-65% success in aphakic and pseudophakic eyes with refractory glaucoma. This, however, is a relative success based on obtaining an IOP equal to or less than 21mm Hg. Today we know that in advanced glaucomas with significant damage to the optic nerve, a target pressure of 21mmHg is unsatisfactory.

For the patients in which the Molteno implant is indicated, however, it is a highly useful device. Molteno has dedicated years of fruitful work to develop the seton and to further modify its design.

The Schocket[4] implant and the long Krupin-Denver[5] implant are similar devices. They consist of a silicone tube coupled to an encircling element, which becomes encapsulated and acts as the reservoir. Results are similar to those reported with the Molteno implant.

The main complication of the trans-limbal equatorial shunt devices is overfiltration during the early postoperative period, leading in some cases to suprachoroidal hemorrhage and choroidal effusion, which are the usual complications of prolonged hypotony. These shunts may also be obstructed by vitreous or uveal tissue.

Overfiltration is due to unrestricted flow of aqueous through the seton tube. Although the Krupin-Denver seton has a valve at the distal end of the tube this does not function very well and allows escape of aqueous at very low IOP. More recently the Ahmed seton and the Baerveldt have become available. See later in this Section Chapters 36 and 37.

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Chapter 36
SURGICAL TECHNIQUE FOR THE MOLTENO SETON

Maurice Luntz, M.D., F.A.C.S.

Surgical Technique for Molteno Implant

The Molteno Single Plate Seton

A fornix-based conjunctival flap is raised over one quadrant of the globe. The quadrant selected depends on the positioning of previous surgery; as the previous surgery has generally been performed in the superior quadrants, one of the inferior quadrants is chosen. The inferonasal quadrant is preferred, as a large bleb is better hidden under the lower lid in this quadrant. A conjunctival fornix-based flap is raised over this quadrant. The rectus muscle at each border of the selected quadrant is isolated, using a muscle hook. A 4-0 silk suture is positioned under each rectus muscle to act as a traction suture. The eyeball is then rotated using the traction sutures, with exposure of the sclera at the operation site. A caliper is set at 8mm and a mark made 8mm back from the cornea at each border of the quadrant, separating these marks 8mm apart from each other. Two preplaced 5-0 Mersilene sutures are then placed through partial thickness of the sclera at each point marked off by the caliper (Fig. 1).

Mitomycin C is used in a titrated dosage followed by copious irrigation using balanced salt solution. The Molteno implant is then removed from its packaging and the base plate inserted along the scleral surface under the conjunctiva and secured with the preplaced 5-0 Mersilene sutures. (**Editor**: The use of mitomycin with setons is controversial).

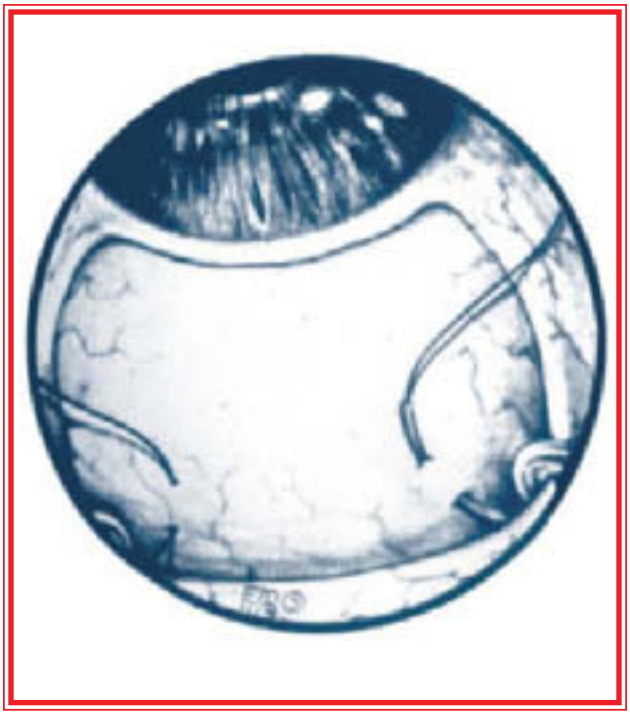


Fig. 1: Fornix based conjunctival flap exposing quadrant of sclera. Pre-placed 5-0 Mersilene sutures 8mm behind limbus and 8mm apart.

Next, the Molteno tube is trimmed to approximately 1.5mm from the limbus inside the cornea. The end of the tube is bevelled with the bevel facing the cornea using Vannas scissors. A 20-gauge needle is used to enter the anterior chamber commencing approximately 1.5mm behind the corneal limbus and directing the needle parallel to the iris surface. (Fig. 2)



Fig. 2: a 4mm x 4mm lamellar scleral flap is raised. A 20-gauge needle makes a tract through the sclera into the anterior chamber, starting 1.5mm behind the limbus.

The needle follows the path of the Molteno tube. It should enter the anterior chamber just anterior to the iris and well behind the cornea. The needle is removed and the tube is threaded through the track and positioned in the anterior chamber just anterior to the iris and well behind the cornea. (Fig. 3). The tube should extend into the anterior chamber approximately half the distance from the corneal limbus to the pupil margin. If the tube is too long, it should be removed, shortened and replaced. The tube is secured with a mattress 10-0 nylon suture parallel to the tube, extending from a point just anterior to the base plate to a point just posterior to the limbus.

A 4 x 4mm square of human processed pericardium (tutoplast from Biodynamics) is placed over the tube and secured to the sclera at each corner with a 10-0 nylon suture. An alternative procedure is to raise a 4 x 4 mm 1/3 thickness lamellar scleral flap and run the tube under this flap, securing it by suturing the flap back over the tube. This method is illustrated in (Fig. 3). The conjunctiva is now anteriorly rotated and secured with a continuous 10-0 nylon suture to the limbus. During the procedure, the anterior chamber remains formed with air or Healon

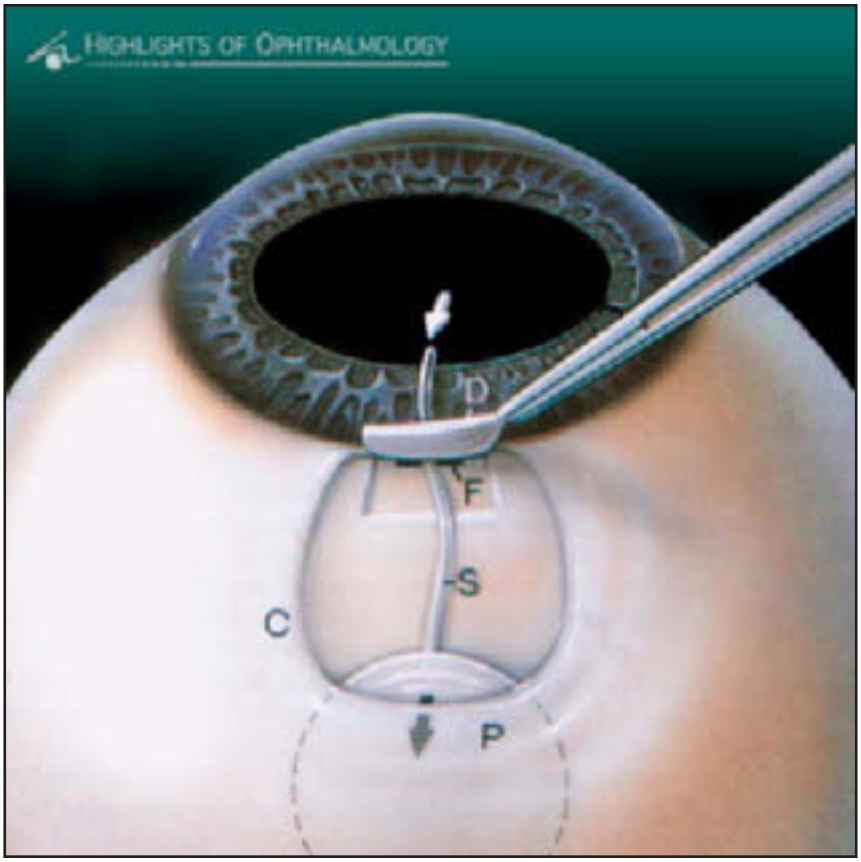


Fig. 3: Seton Implantation Procedure

A fornix based conjunctival flap (C) is raised and the methylmethacrylate baseplate (P) of the Seton is pushed under the conjunctival flap posteriorly and sutured to the scleral surface. The implant has a biconcave shape with the inferior surface shaped to fit the sclera. A small 3mm square half thickness lamellar scleral flap (D) is raised just as in a trabeculectomy. An incision (F) is made into the anterior chamber under this scleral flap and the long silicone tube (S) of the Seton is placed into the anterior chamber (the end of the silicone tube can be seen in the anterior chamber near the tip of the white arrow). Next, the scleral flap (D) is sutured down around the tube (S) of the Seton. Finally, the conjunctiva is sutured back in place. Aqueous then drains from the anterior chamber (white arrow) down through the tube (S) to the baseplate (P) (black arrow), where a bleb forms.

Double-Plate Seton

In patients with extensive conjunctival scarring and in African-American patients a double-plate seton is used. The second plate, which is joined by a silicon tube to the first plate is sutured to the sclera in an adjacent quadrant following the same technique used for the first plate. The tube that enters the anterior chamber is attached to the first plate.

Chapter 37
SURGICAL TECHNIQUE FOR THE BAERVELDT SETON IMPLANTATION

George Baerveldt, M.D.

Description of the Baerveldt Glaucoma Implant

The design of the Baerveldt glaucoma implant was based on a desire to perform glaucoma implant surgery through one quadrant and utilize large surface area glaucoma implants that produce minimal irritation to the intra and extra ocular tissues and obtain intraocular pressures in the low teens.

Medical grade silicone has been used extensively in ophthalmology as it is flexible and produces minimal tissue reaction. The Baerveldt glaucoma implants use silicone that is barium impregnated to displace unbound silicone oil and allows radiological identification of the glaucoma implant. Barium combined with gamma irradiated increases the polymer cross linkages and allows for the manufacture of the thinnest possible plate while still maintaining rigidity and flexibility. The plate is 0.9 mm thick and is the lowest profile glaucoma implant manufactured. The implant is tumble polished to produce an extremely smooth surface with a low wetting angle that allows the implant to move smoothly and freely in the subtenon's space when it is implanted.

The Baerveldt glaucoma implant consists of a non-valved silicone tube (0.64 mm external diameter with a 0.30 mm internal ball) that is attached to a plate. The newest plates are kidney shaped. Anteriorly there is a straight ridge that divides the flange from the convex surface of the plate. The anterior flange has two large suture holes. The tube crosses the small flange area and passes through the ridge with the tube opening on the posterior surface of the ridge. The straight 10-mm long ridge was designed to be used for patients with encircling elements from previous retinal surgery. The fibrous capsule surrounding an existing encircling element is opened in one quadrant. The surgeon amputates the shoulders of the implant and slips the implant between the sclera and the encircling band or scleral buckle to produce a modified Schocket procedure (Fig. 1).

The 250 Model consists of a plate that is 22 mm at greatest length and 15 mm broad. The total surface area of the plate is 260 sq. mm + 5 mm. The 350 Model is 32 mm in length and has a width of 14 mm with a surface area of 343 mm + 7 mm.

The pars plana Baerveldt glaucoma implant was designed for use in patients who have undergone a previous vitrectomy or who require a vitrectomy and simultaneously glaucoma implant[5,6]. The Hoffman elbow consists of a small episcleral plate with two suture holes. A 5.1-mm semi-rigid, tapered, and beveled cannula is angled posteriorly at 105º to prevent lenticular contact should the patient be

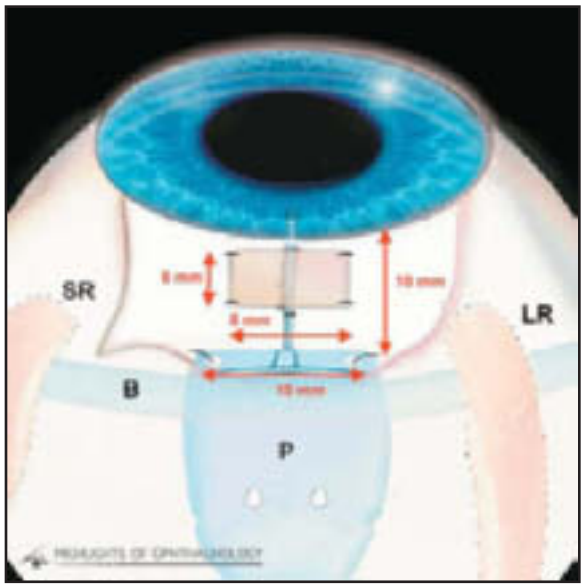


Fig. 1: Modified Schocket procedure with the plate (P) positioned between the sclera and encircling band (B) after the shoulders have been amputated.

phakic. The 5.1-mm cannula is introduced through the 20-gauge M.V.R sclerostomy site that has been utilized to perform the vitrectomy. The length of the tube is 7 mm measured from the suture holes of the pars plana elbow to the holes of the 350 plate.

The bleb height that forms around glaucoma implants is dependent on the width of the implant. With a large surface implant, a large bleb forms and produces a large space-occupying mass in the orbit. The mass effect can produce an incomitant strabismus by limiting movement of the eye in the direction of the implant. Equidistantly spaced fenestrations in the center of the implant halve the width of the implant by allowing fibrous scar tissue to rivet the scleral to the conjunctival surface of the bleb. These fenestrations have dramatically decreased the volume and height of all blebs.

Indications for Baerveldt Glaucoma Implants

Patients who qualify for glaucoma implants usually have failed antimetabolite filtering surgery. Glaucoma implants are used as the primary surgical therapy in neovascular glaucomas or patients whose conjunctiva precludes the use of a trabeculectomy. The pars plana implant should be considered in neovascular glaucoma with traction retinal detachment or if the media precludes sufficient panretinal photocoagulation. A pars plana vitrectomy, endophotocoagulation and long acting gas tamponade has increased the long term success rate with decreased early postoperative complications due to stabilization of the retinal disease. Anterior segment indications include lack of space, aphakic with vitreous in the anterior chamber or other abnormalities that preclude placement in the anterior chamber.

Surgical Technique

The patient is given a full examination with careful consideration to the quadrant into which the glaucoma implant is to be inserted. The most desirable quadrant for implantation is the suprotemporal followed by the superonasal quadrant as pseudo-Browns syndrome has been reported following glaucoma implant surgery in the supronasal quadrant. The infronasal or the infro temporal quadrant is the next choice. Glaucoma implants with a high ridge have been reported to catch on the inferior orbital rim causing the inability to elevate the eyes and the implant with the lowest ridge should be sutured 10-12 mm posterior to the limbus if the inferior quadrant is chosen.

Description of Surgical Technique

If a limbus based conjunctival flap is used, the incision is made 3 to 4 mm posterior to the limbus in the desired quadrant (Fig. 2). Approximately

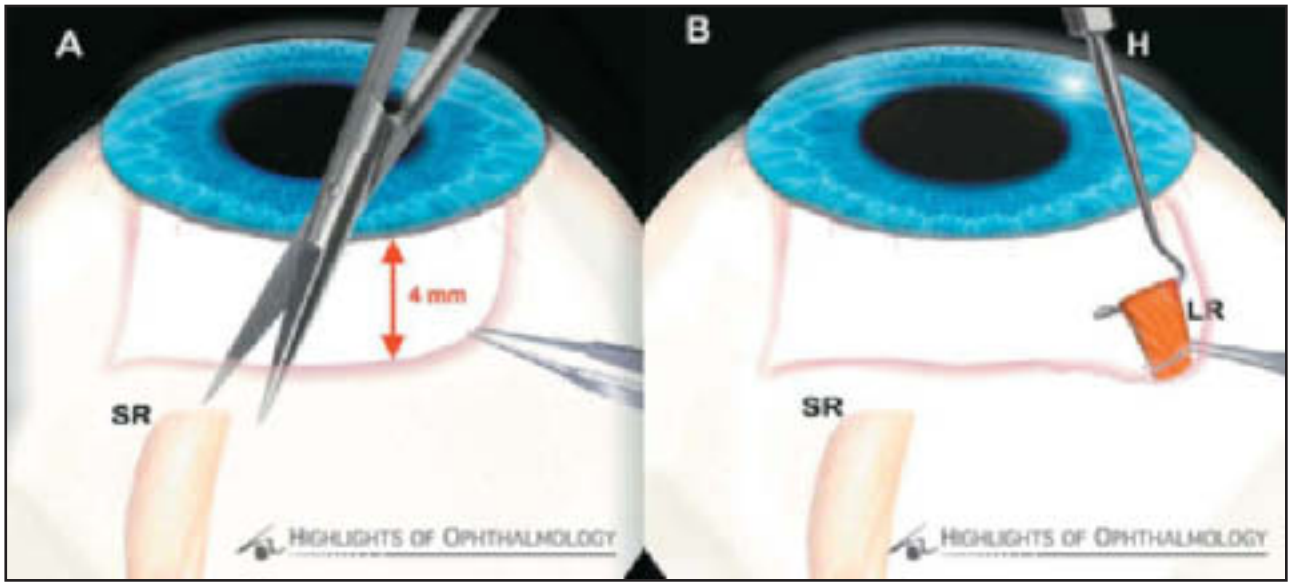


Fig. 2: (A-B): Limbus based conjunctival flap dissected 4mm posterior to the limbus the superior rectus is isolated. Stripping of Tenon's capsule from the lateral rectus muscle (LR) after being isolated with a muscle hook (H).

120º of conjunctiva is incised and the conjunctiva and Tenon's capsule is mobilized to the limbus. The posterior Tenon's capsule adherence between the recti muscles is dissected free from the underlying sclera with blunt dissection. If a fornix based conjunctival flap is utilized, a 120º limbal incision is made with a relaxing incision large enough to allow easy access to the muscle insertions.

If the IOP is excessively elevated, a paracentesis should be performed at the beginning of the surgery and the eye slowly decompressed. Insertion of the implants is facilitated if the IOP is kept around 15 to 25 mm Hg.

Different techniques are utilized for the different models. For the Baerveldt 250 model, the eye is rotated inferiorly using a muscle hook to engage the superior rectus muscle. The Baerveldt 250 glaucoma implant is grasped longitudinally with a large non-toothed forceps. The implant is inserted longitudinally between the two recti muscles and then rotated so that the flange lies between the recti muscles.

The Baerveldt 350 glaucoma implant was designed to be inserted between the sclera and posterior to the recti muscles insertions. The superior rectus muscle is isolated with a muscle hook (Fig. 2) and Tenon's capsule surrounding the muscle is stripped from the muscle belly by sliding Tenon's capsule posteriorly along the muscle. A second muscle hook is employed to lift the rectus muscle belly

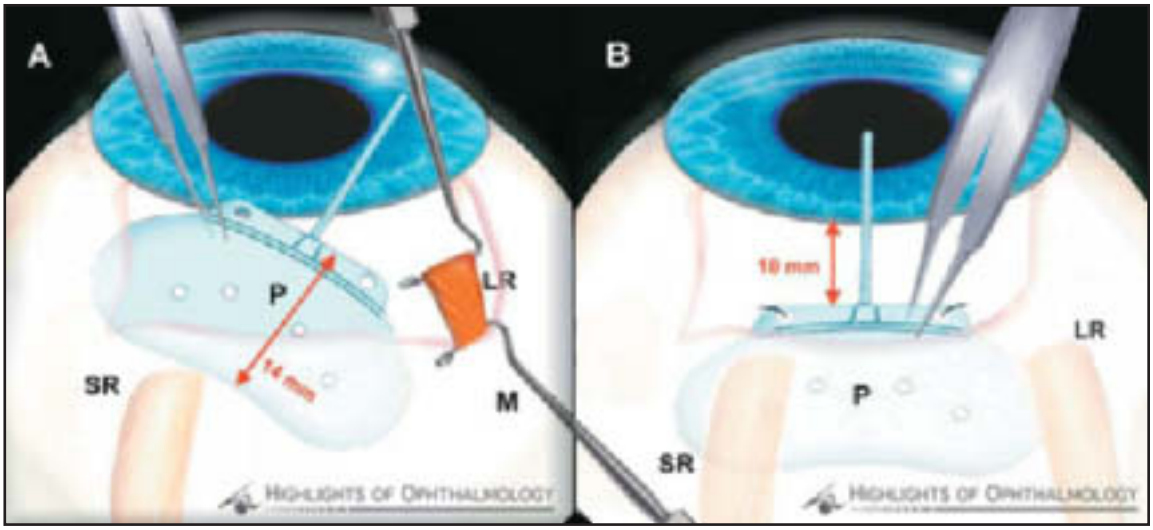


Fig. 3 (A-B): Scleral pocket created with a second muscle hook (M) elevating the muscle belly from the sclera. The positioning of the flange between the recti muscle insertions of a model 2.50 implant (P). The glaucoma implant is sutured to the underlying sclera with 2 non-absorbable sutures.

from the sclera so that a pocket is created (Fig. 3). The implant is grasped longitudinally with a large non-toothed forceps and 70% of the implant is then inserted posterior to the muscle insertion (Fig. 3). Similarly, the lateral rectus is isolated with muscle hooks. The implant is now advanced beneath the muscle until the flange lies between the recti muscle insertions (Fig. 3).

A caliper is used to confirm that the anterior edge of the implant is 10 to 12 mm posterior to the limbus. This allows the implant to be positioned 2-mm posterior to the muscle insertion.

The thinnest sclera is located just posterior to the muscle insertions and great care must be made not to perforate the globe with a suture. I use a 7-0 Prolene non-absorbable suture on a BV 1 needle. The first suture should be placed as close to the superior rectus muscle as possible and the knots buried in the suture holes (Fig. 3). The suture near the lateral rectus muscle must pull the implant so that it is hammocked against the sclera with no anterior or posterior movement after the sutures have been tied. If the sclera posterior to the muscle insertions is staphylomatous or the patient has scleritis, the 7-0 Prolene sutures can be passed through the recti muscle tendons at their insertions and the implant hammocked between the muscle insertions thus preventing perforation of the sclera.

As these are non-valved implants, the tube needs to be ligated 1 to 2 mm anterior to the implant flange with a 7.0 or 8.0 absorbable suture (polyglactin). To insure total occlusion, a 30-gauge cannula is inserted into the tube and back flushed with saline (Fig. 4). Two or 3 passes of the polyglactin needle are made through the tube anterior to the tube ligature to produce leakage. An alternative method of tube occlusion is to thread 5 mm of a Prolene suture through the distal end of the tube. Ligate the tube 2 to 3 mm anterior to the flange with a 7-0 absorbable suture so that the tube is occluded around the Prolene suture. The needle of the Prolene suture is then passed subconjunctively and inferiorly so that the suture exits the conjunctiva 4-mm posteriorly to the limbus in the inferior fornix. The suture is cut flush with the conjuctiva at the end of surgery. The suture is retrieved when desired by cutting down through the conjunctiva and removing the suture. This technique is known as the "ripcord technique".

The tube can be curved and sutured to the underlying sclera to gain the desired entry site into the anterior chamber. The tube is now draped over the cornea. It is cut 1 to 2 mm anterior to the limbus with the bevel facing up (Fig. 4).

It is advisable to cut the tube slightly longer as the tube can always be trimmed. A paracentisis must be made prior to making the tube needle inci-

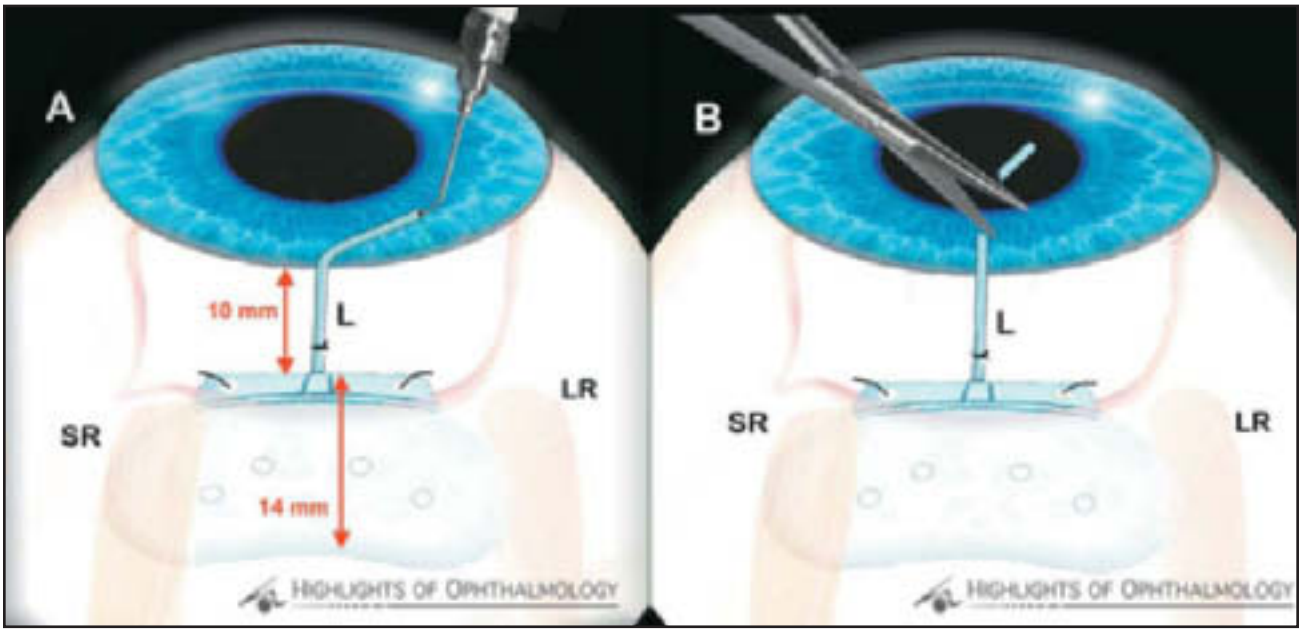


Fig. 4: (A-B): Total occlusion of the ligated tube (L) is checked prior to making needle passes through the tube. The tube is cut to the desired length with the bevel facing up.

sion (Fig. 5). It is important that the tube does not touch the cornea and lies as far posteriorly from the cornea as possible. The anterior chamber is deepened with balanced salt. A 22-gauge needle on a syringe with the bevel facing posteriorly makes a tract into the anterior chamber approximately 1/2 mm posterior to the limbus. The needle must be aimed parallel with the iris plane (Fig. 6). Should the anterior chamber shallow, inject saline. Assess the position on the needle. If it is too close to the cornea, a step ladder technique of re-introducing the needle in 1/4 mm steps posteriorly to obtain excellent needle position without injury to the iris or lens. The tube is then inserted. The ideal tube length is approx-

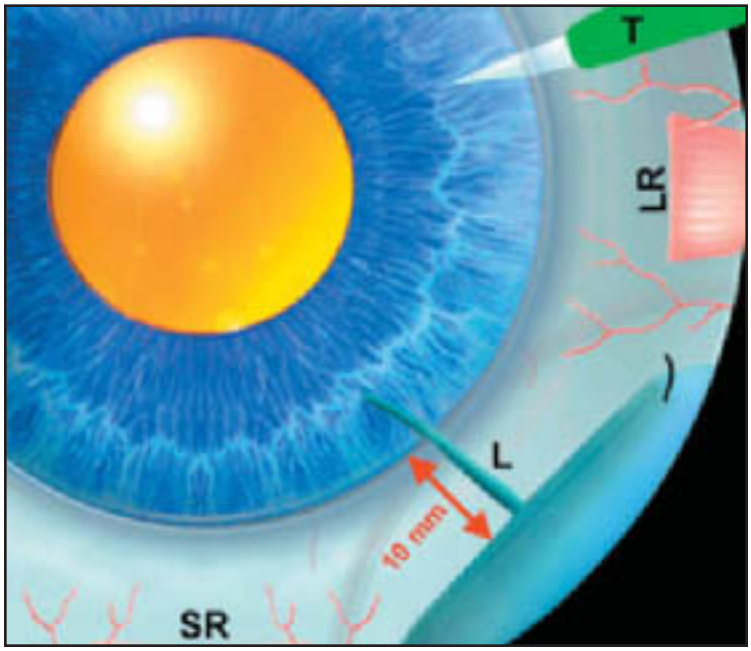


Fig. 5: Paracentesis tract (T) is performed prior to placement of the tube (L) in the anterior chamber.

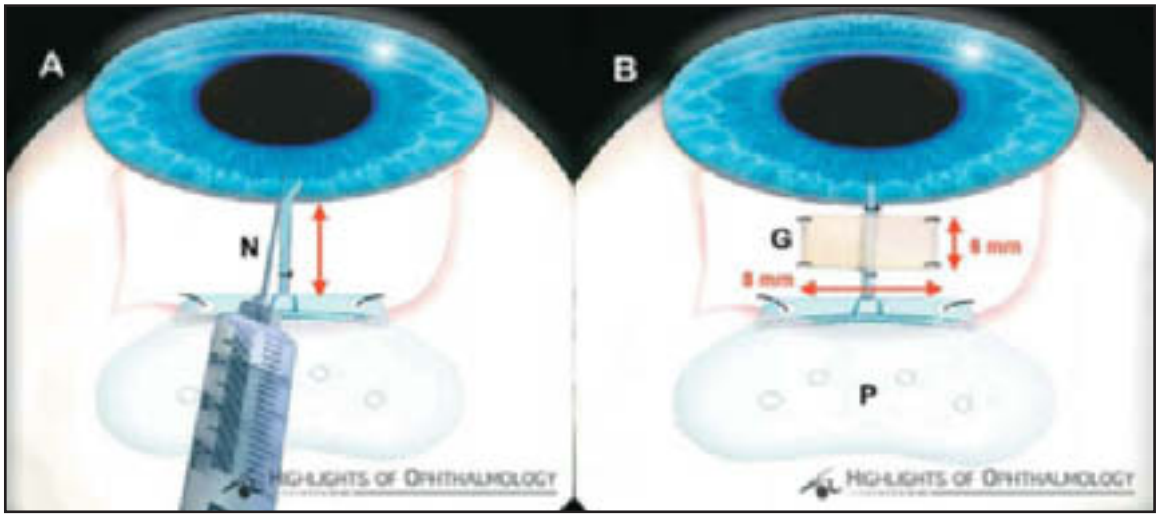
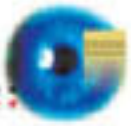


Fig. 6: (A-B): Twenty-two gauge needle (N) with bevel facing down is used to make an entry site into the anterior chamber with the needle parallel with the iris. The tube in the anterior chamber and covered by a connective tissue graft (G) the implant (P) is secured in proper position. Closure of Tenon's capsule with a running absorbable suture followed by closure of the conjunctiva with a running absorbable suture.



imately 1 1/2 mm in the anterior chamber. If the tube is too long it is withdrawn and trimmed. The exception is neovascular glaucoma where the tube tip should be positioned in the pupillary space.

A connective tissue graft, such as sclera or pericardium is employed to cover the tube. Suture the tissue graft to the underlying sclera with 4 absorbable sutures (Fig. 6). Tenon's capsule is closed with a running 7 or 8-0 polyglactin suture (Fig. 6). If the anterior Tenon's capsule is very thin, the posterior Tenon's capsule can be pulled anteriorly and sutured to the episclera and the connective tissue graft. The conjunctiva is then closed separately with a running absorbable suture (Fig. 6).

Antibiotics and steroids are administered subconjunctively and the eye is patched. The patient is started on topical antibiotics, steroids, and mydriatics the following day. The steroids are tapered as the injection of the conjunctiva decreases. The IOP can be controlled, if necessary, by restarting the preoperative glaucoma medications. In neovascular glaucoma patients the "ripcord" can usually be safely removed after the first week in patients with florid rubiosis. In the majority of patients the "ripcord" usually is removed between the third and sixth week postoperatively. The 8-0 polyglactin tube occlusion suture normally releases between 2 to 4 weeks and the 7-0 polyglactin suture releases around 4 to 5 weeks. Suture lysis can be utilized to rupture the 7 or 8-0 polygalactic sutures at an earlier date. For this reason do not cover the suture with the connective tissue graft or cut a notch in the connective tissue graft so that, if it becomes necessary, this suture can be lasered.

Results

There have been only 2 randomized prospective glaucoma implant studies performed. Both these studies used a similar patient population. The randomized patients were pseudophakic, aphakic or had failed a trabeculectomy surgery. The first study compared the single plate (135 mm) Molteno implant to the double plate (270 mm) Molteno implant [1,2]. At 2 years there was a 46% life table success rate with the single plate Molteno implant as compared to 71% success rate with the double plate Molteno implant. Based on these figures I designed 3 different sized Baerveldt glaucoma implants. The 250, 350, and 500 models. The 250 model was based on the results obtained with the double plate Molteno implant. As the surface areas closely approximate each other it is not surprising that the 250 model has similar long-term outcomes as the double plate Molteno implant.

To assess outcomes of even large surface implants, another randomized prospective study was initiated[3,4]. The Baerveldt 350 models were designed to be 3 times the surface area of a single plate Molteno implant. The largest size implant that could be manufactured to be introduced through 1 quadrant was 500 mm2 or 4 times a single plate Molteno implant. It was hoped that this prospective randomized trial would indicate the "ideal" surface area for the majority of patients who require glaucoma implants. Life table analysis at 5 years shows that the 350 model achieved a 79% success rate as compared to a 66% success rate with the 500 model. The 350-model implant obtained a 13.7-mm median pressure on one medication and the 500 model a 13.1% on 1.6 medications. Based on this data, the "ideal" surface area for the majority of advanced glaucomas is the Baerveldt 350 model. The 450 and 500 model implants have been discontinued.

The Baerveldt pars plana glaucoma implant used in conjunction with a vitrectomy and gas tamponade has a 24 month success rate in neovascular glaucoma of 72% and in non-neovascular glaucoma a 92% success rate [5,6,7].

Conclusion

Significantly lower IOP's and increased success rates are obtained with the Baerveldt 350 glaucoma implant. This implant requires fewer medications to maintain the IOP below 16-mm Hg. The 250 model should be used in eyes with a decreased aqueous production, especially patients with uveitis or a history of previous cyclodestruction. Combining pars plana vitrectomies, endophotocoagulation, stabilizing traction detachments, and utilizing long acting gas tamponade with the pars plana implant has significantly increased the long term success rates in neovascular glaucoma and has decreased the complications.

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Chapter 38
SURGICAL TECHNIQUE FOR AHMED GLAUCOMA VALVE IMPLANTATION

Craig H. Marcus, M.D.

The Ahmed Glaucoma Valve Implant has gained widespread use because it affords two distinctive advantages compared with other tube shunts. First and foremost it supplies a dependable valve system that when implanted properly virtually eliminates shallow or flat chambers in the early post operative period, thereby avoiding the need to occlude the tube or use a two-staged procedure. Second, its single quadrant design avoids any muscle manipulation for insertion. Recently, a double-plate, two quadrant design, Ahmed Glaucoma Valve has been introduced for larger surface area.

The Ahmed Valve polypropylene plate is 184 mm^2 that conforms to the shape of the globe. It is 16 mm in length, 13 mm in width and 1.9 mm in height. The valve system is housed in the anterior third of the plate and consists of a folded membrane inside of a tapered chamber, that is designed to open at 8 - 10 mmHg. There are two fixation eyelets used for anchoring at the anterior edge of the plate. The tube is made of silicone and is compatible with a 23 gauge needle.

The second plate of a double-plate system has no valve but also has two fixation holes. It can be connected to either side of the valved plate approximately midway by a tube that can ride under or over the intervening rectus muscle. It provides an additional 180 mm^2 of surface area for a total surface area of 364 mm^2.

The indications for the Ahmed Glaucoma valve tube shunt use are based on the surgeon's discretion, but, essentially include any situation where anterior conjunctival cicatrization is likely to overcome traditional glaucoma filtration surgery. General case guidelines would include: two or more failed traditional glaucoma filtration surgeries, active rubeotic glaucoma, combined penetrating keratoplasty, aphakic infantile glaucomas, uveitic glaucomas, and other complicated glaucomas.

The procedure can be conceptually segmented into 5 components: 1) conjunctival dissection; 2) securing of primed valve implant to the sclera; 3) tube insertion; 4) covering of patch graft over the tube; and 5) conjunctival closure. Each will be discussed in detail.

Site of Surgery Selection

Inspection of the eye prior to surgery is helpful in determining the best intended location for the implant and the tube. The superotemporal quadrant is ideal because it is protected by the upper lid, is anatomically accessible, is devoid of oblique muscles, and in neovascular cases avoids tube clogging by any bleeding (some of which is expected). (Some surgeons prefer placement in the infero-nasal quadrant as a large bleb is less irritating and less visible in that quadrant and gravity may be helpful - **Editor**). The conjunctiva must be carefully inspected for mobility. Completely matted conjunctiva may require implantation inferotemporally or in another quadrant. It may even preclude implantation altogether. The anterior chamber depth

and iridocorneal adhesions must by identified. These may require synechiolysis, movement of the tube into another quadrant, or placement of the tube posterior to the iris. An advantage to posterior placement of the tube is that it is far removed from the corneal endothelium and therefore is unlikely to harm it; however, visibility of the tube is reduced or possibly eliminated and blockage with vitreous may occur.

When confronted with an aphakic eye it is often most desirable to use a pars plana approach for the tube site. In this situation a thorough vitrectomy including trimming of the vitreous skirt is required; and therefore a virtreoretinal surgeon should join the glaucoma surgeon in performing this portion of the surgery. (Some surgeons prefer placement through the pars plana approach. The author and editor prefer the anterior chamber - **Editor**.)

Technique

A disposable contact lens or collagen shield along with a cut cellulose sponge or corneal cover provides maximal corneal protection and is strongly recommended in a post- corneal transplant situation. For scarred conjunctiva a sub-Tenon's injection of lidocaine with epinephrine on a 25 gauge needle make for an easier dissection and provides some additional hemostasis. A fornix based conjunctival flap provides excellent exposure, although some prefer a limbal based or midway incision. Wescott scissors are used to dissect the conjunctiva at the limbus and relaxing incisions are made approximately 135 degrees apart. Conjunctival dissection should proceed further than the relaxation incisions so that some stretching of the conjunctiva is possible to adequately cover the implant. Steven's scissors are useful for the more posterior quadrantal dissection. An 8-0 nylon traction suture can be placed 3 - 4 mm posterior to the limbus in the center of quadrant directly in the intended path of the tube. The globe then is rotated by clamping the 8 - 0 nylon suture and posterior dissection is completed (Fig 1). Gentle cautery is applied to the area along where the tube will course. Some surgeons advocate the use of mitomycin C, 12- 16 mm posterior to the limbus at this point. For the use of a double-plate technique an

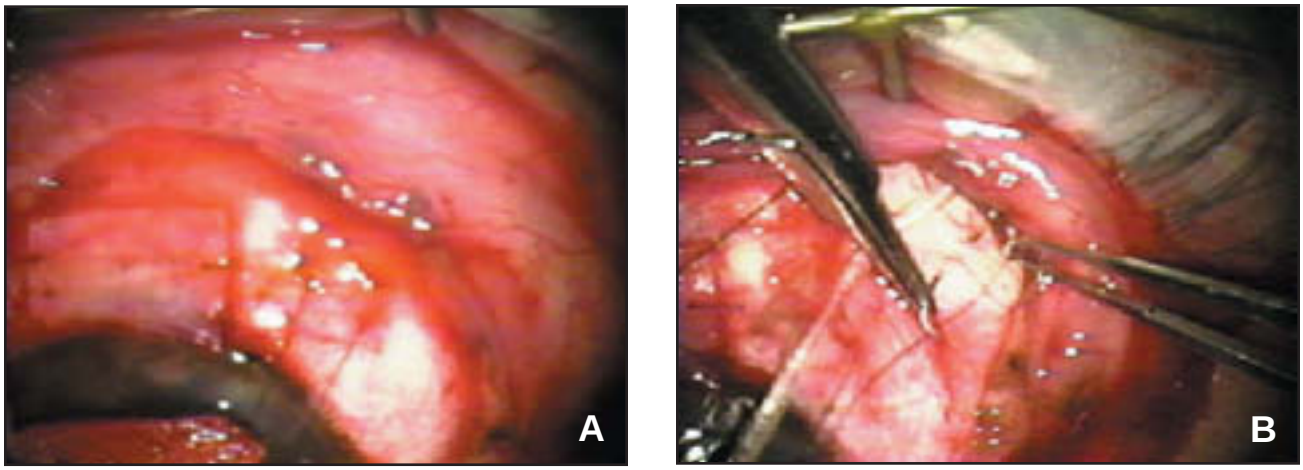


Fig. 1 (A-B). Fornix-based conjunctival flap has been raised in the superotemporal quadrant and two relaxing radial incisions made approximately 135 degrees apart. The conjunctiva has been dissected as far back as possible to prepare a bed for the implant. An 8-0 nylon traction suture has been placed 3-4mm posterior to the limbus in the center of the quadrant and clamped to the sterile towels superiorly after rotating the globe upwards.

adjacent quadrant is prepared. Special care must be taken to dissect Tenon's away from the muscle between the plates.

After the Ahmed Glaucoma Valve is primed with 2 cc of Balanced Salt Solution (BSS) on a 27-gauge cannula the conjunctiva is gently lifted and the implant is grasped between the index and forefinger and placed into the sub-Tenon's space. Viscoelastic can be placed over the surface of the distal end of the plate makes sliding the implant into the space somewhat easier. Once the implant is approximately halfway underneath the conjunctiva a .12 forceps can be used to grasp one of the eyelets or alternatively the unclosed forceps placed at the anterior junction of the plate where it is connected to the tube and the plate is pushed posteriorly to ensure that the dissection is adequate. The plate then is pulled forward so that each of the eyelets can be identified and an 8 - 0 nylon suture threaded through each of them (Fig 2). The suture is then passed through 1/3 thickness of scleral and secured to the globe 8 - 10 mm posterior to the limbus (Fig 3). With this method the knots are underneath the eyelets preventing erosion through the conjunctiva.

For a double plate procedure the connecting tube is attached prior to securing the valved plate to the sclera and the second plate is then secured to the globe in the adjacent quadrant.

At this point the traction suture is released and attention turned to the anterior segment. A paracentesis is performed and the globe made slightly more firm with injection of viscoelastic so that the needle tract into the eye will be easier. It is important, however, not to deepen the chamber falsely, thereby distorting the anatomy and causing too deep a placement of the needle tract. In neovascular glaucomas it is advisable to inject viscoelastic at the intended site of entry into the eye (if in the anterior chamber) and to

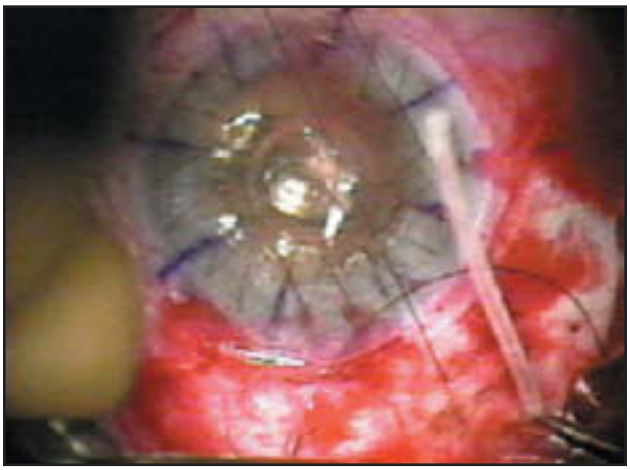


Fig.2. The plate has been pushed into the subconjunctival pocket prepared as in Fig.1, with the anterior eyelets exposed. An 8-0 nylon suture has been threaded through each eyelet.

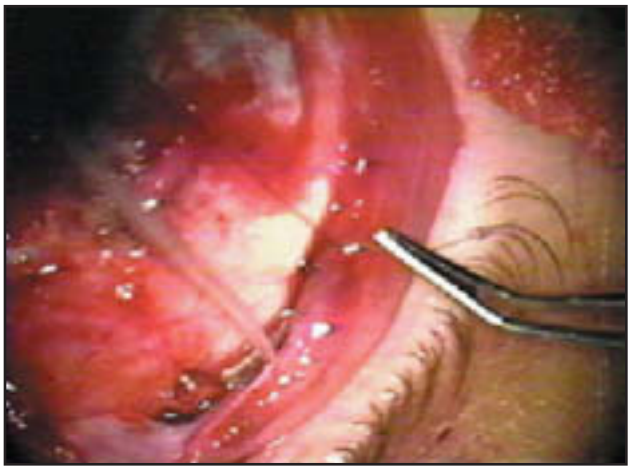


Fig. 3. The suture placed through each eyelet has been passed through one-third thickness of the sclera between 8 to 10mm posterior to the limbus and tied under the implant.

lyse the adhesions at this point. There will likely be some bleeding; however, the viscoelasitc will tamponade. The original 8 - 0 nylon traction suture is then used in reverse to stabilize the eye by grasping the suture between two fingers or with a needle holder. A 23- gauge needle is then used to enter the anterior chamber just short of 1.5 mm posterior to the limbus. The course of the needle should be parallel to the iris and just anterior to it (Fig 4). In eyes with scarred corneas it is important to carefully view the course of the needle and observe it in the anterior chamber because viewing the tube itself may be difficult. The tube then is trimmed to a 2 - 3 mm anterior chamber length (remembering that re-trimming the tube is much easier than lengthening it) with a bevel-up orientation and inserted through the needle tract. A small amount of viscoelastic into the needle tract can ease the tube placement. To insert the tube use of a specialized forceps (designed by Fechtner) or use of a straight non-toothed forceps to introduce the tube and an angle forceps to support the tube 2 mm posterior to the point of entry makes insertion easier. Occasionally this step can be tedious. The position of the tube is checked and re-trimmed if necessary. A second instrument such as an iris sweep or a viscoelastic cannula inserted through a paracentesis can aid in lifting the tube away from the iris or gently coaxing it over an anterior chamber intraocular lens if necessary. A 10 - 0 nylon suture is then used to secure the tube to the globe (Fig 5). This suture can also be used to shorten the intraocular length of the tube although a second 10-0 nylon suture may be needed to attached any curved extraocular tube portion to the sclera so that the extraocular profile of the tube will be as flat as possible.

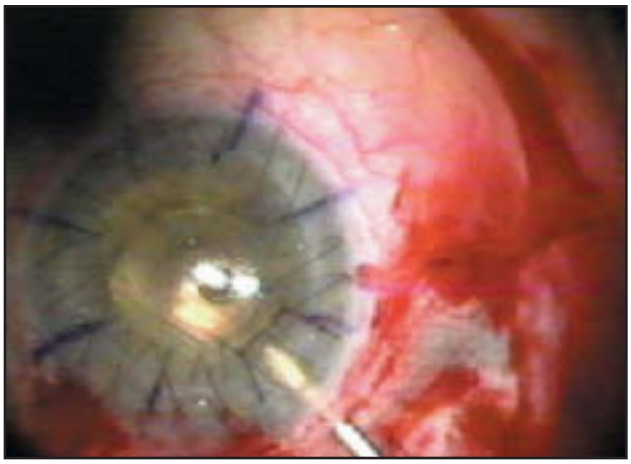


Fig. 4. A 23-gauge needle attached to a 5cc syringe enters the sclera 1.5mm posterior to the limbus and is advanced into the anterior chamber parallel to the level of the iris. The 5cc syringe is filled with BSS or viscoelastic and injected into the AC, if the AC shallow or collapses.

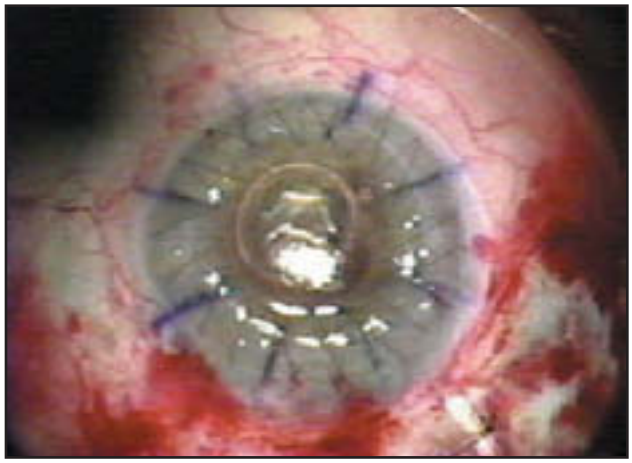
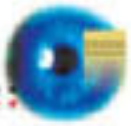


Fig. 5. The Ahmed valve tube is secured to the sclera by a 10-0 nylon suture.



For the pars plana insertion the needle tract should also be parallel to the iris. If good dilation is possible then a 2-3 mm intraocular tube length is ideal. For poorly dilating pupils a slightly longer intraocular length may be important for future visualization of the tube. In pediatric cases sufficient length of the tube in either the anterior of posterior position is important to accommodate future growth of the eye. This extra attention will help avoid the possibility of the tube being withdrawn from the eye and thereby the necessity for a tube lengthening procedure.

Since the tube would likely erode through the overlying conjunctiva if left unprotected, it is wise to use either a patch graft of sclera or pericardium, or alternatively make a partial thickness scleral pocket. Pericardium (Tran Z Graft or Tutoplast) provides excellent tensile strength and is easy to manipulate. Two to four 8 - 0 or 9-0 vicryl sutures are used to secure the patch graft to the globe. Some have used scleral allografts for this purpose.

The conjunctiva is then returned to its original anatomical position using 8 - 0 vicryl in a running fashion. Unlike a trabeculectomy this closure need not be water tight because the filtration is far posterior to the limbus, although it should not be cavalier. Special care should be taken to be sure that the patch graft tissue is covered snugly to avoid dellen formation. Sometimes the conjunctiva becomes edematous and coverage of the implant and patch graft seems impossible; however a wet cotton-tipped applicator can be used to comb forward and stretch the conjunctiva.

Viscoelastic should be gently irrigated out of the anterior chamber but may be left in for neovascular glaucoma cases or when hypotony is expected or greatly feared. With superior quadrant tube placement in neovascular glaucomas or if bleeding from the needle pass has occurred it is useful to place an air bubble in the anterior chamber to tamponade the site of bleeding. Almost invariably hypotony is technique-related by creating too large an opening of the needle tract or may be tissue related, especially in pediatric cases where it is more elastic. Sometimes it is useful to cannulate the tube in the anterior chamber with a 27- or 30-gauge cannula and to irrigate it and observe posterior bleb formation.

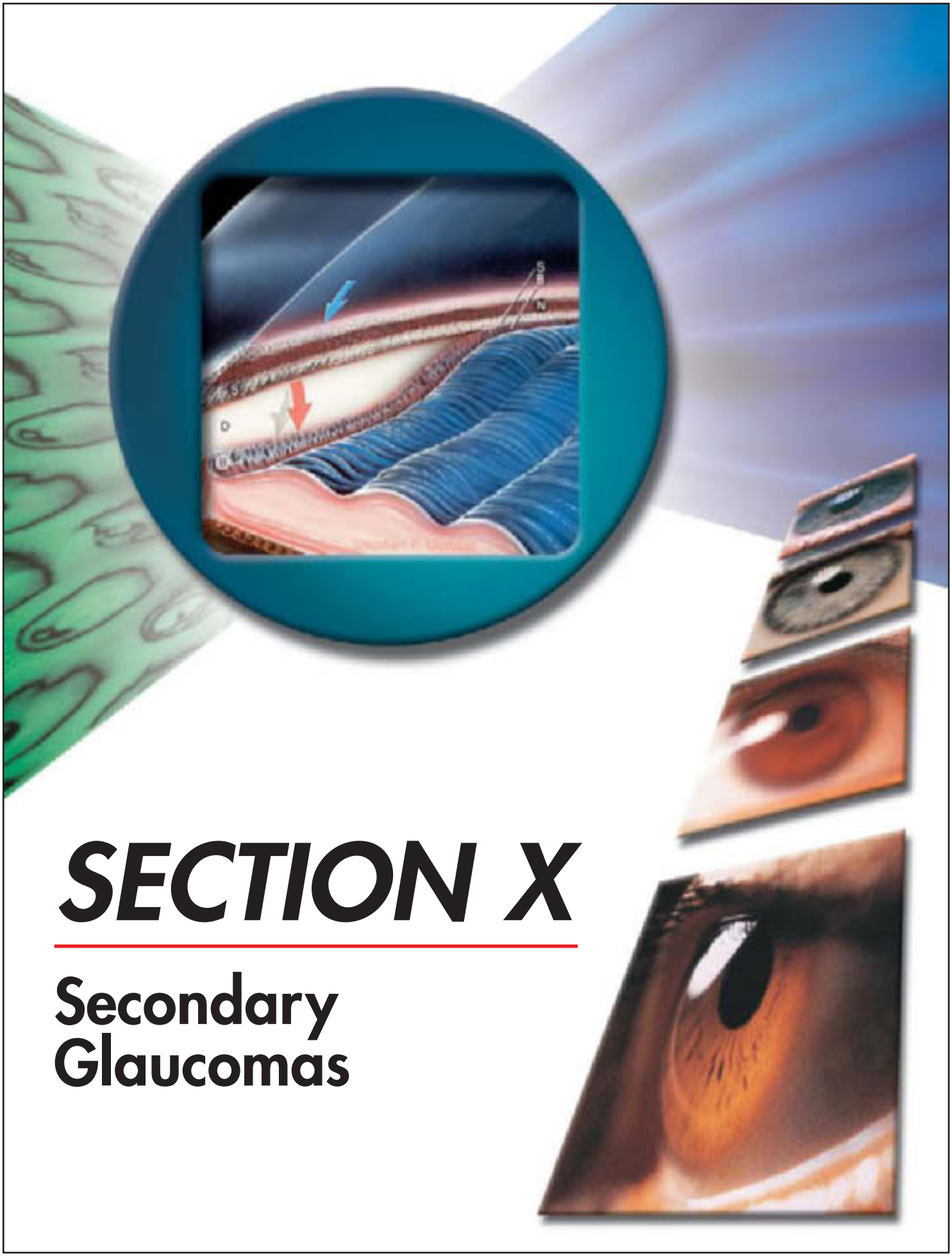
Subconjunctival injections of solumedrol and antibiotic of choice, instillation of ointment, and placement of a patch and shield are performed. The patient usually will be comfortable without requirement of analgesics and is examined on the first postoperative day and followed closely thereafter.

In the early post operative period if the rare occurrence of hypotony is noted then viscoelastic can be injected into the anterior chamber. If pressure elevation is noted then either bleb needling can be performed or the tube can be cannulated and irrigated using a syringe with BSS if tube occlusion is suspected. If heme or fibrin has occluded the tube then tPA (6-12 micrograms) can be flushed through the tube at least five days postoperatively.

In summary the Ahmed Glaucoma Valve device is simpler to implant than other tube shunt procedures that require extraocular muscle manipulation, provides immediate intraocular pressure control, prevents early postoperative hypotony without the need for additional surgical maneuvers, and provides excellent results.

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SECTION X

Secondary Glaucomas

Chapter 39
SECONDARY GLAUCOMAS

Benjamin F. Boyd, M.D., F.A.C.S.
Maurice Luntz, M.D., F.A.C.S.

GLAUCOMA IN APHAKIC AND PSEUDOPHAKIC EYES

Because there are a variety of mechanisms that cause glaucoma in the aphakic eye, **Luntz** and **Harrison** consider that it is more accurate to speak of glaucoma in the aphakic or pseudophakic eyes rather than aphakic glaucoma. The choice of treatment will, therefore, depend in part on the pathogenesis of the raised pressure. **Complicated cataract extraction is the most common cause of secondary glaucoma**.

Relation Between Increased IOP and Retinal Vein Occlusion

It is important to keep in mind that in eyes with normal discs and visual fields with intraocular pressures persistently over 25mm Hg in patients over 60 years of age, there is a high incidence of **retinal vein occlusion**. Therefore, **we must be very careful to monitor intraocular pressure following cataract surgery to keep the IOP below 25mm Hg**. Otherwise, we may end up with the occasional eye which is well operated but cannot see better than 20/200 because of the development of a retinal vein occlusion early in the postoperative course. Considering that most of these patients are on topical corticosteroids in the early postoperative period, if there is any evidence of increased intraocular pressure we must administer a beta-blocker and/or a prostaglandin analogue topically.

Relation Between Glaucoma and Cataract Surgery

In most cases the glaucoma, unless present prior to cataract extraction, is the result of technical problems related to the cataract surgery and can often be prevented by detailed attention to the surgical technique at that time.

Most aphakic or pseudophakic patients who have glaucoma can be adequately controlled with **topical** medications. If they can not, then they enter into the category of high-risk patients for glaucoma surgery that merit the use of antimetabolites (mitomycin or 5-FU) when a filtering operation is performed.

Types of Glaucoma in Aphakic and Pseudophakic Patients

Although aphakic eyes are not often seen, there are still many patients who come to our office who had cataract surgery many years ago and are aphakic.

Glaucoma may predate the cataract extraction. Primary open angle glaucoma, angle closure glaucoma - pupil block - (whether an acute attack,

repeated subacute attacks or chronic angle closure glaucoma with or without peripheral anterior synechiae) and secondary glaucomas may all produce post-cataract extraction glaucoma. In open angle glaucoma sometimes the glaucoma is alleviated by the cataract extraction, but in many cases the glaucoma is not helped or may even become worse.[1, 2]

Luntz has pointed out that congenital, infantile and juvenile glaucomas in which the cataract may be an associated developmental anomaly or a complication of the glaucoma surgery may also present with high intraocular pressure following cataract extraction.

Medical Therapy

Standard medical therapy must be modified when treating glaucoma in aphakic and pseudophakic eyes. The degree of secondary angle closure greatly influences the prognosis. If extensive angle closure is present, medical therapy is rarely successful. (See also chapters 8, 9 – Medical Therapy for Glaucoma.)

Beta-blockers are the commonly used first-line agents. Prostaglandins (Lumigan and Travatan - **Editor**) and Latanaprost are increasingly used as first-line or second-line drugs.

Direct-acting cholinergic medications such as pilocarpine and carbachol can be very effective in pseudophakic and aphakic eyes if the angle has remained open. In the presence of significant synechial angle closure miotics may be ineffective or may result in an increased IOP resulting from pupillary block. Chronic miosis may decrease visual acuity in patients with posterior capsule opacities or subluxated intraocular lenses. The stronger indirect anticolinergics such as echothiophate iodide also can be very effective, and these drugs have the advantage of a once- or twice-daily dosage.[3] Retinal detachment is more common in the aphakic eye and can be a rare complication of strong miotics.

Epinephrine compounds may be used with caution in the aphakic and pseudophakic eye. Long-term therapy may lead to cystoid macular edema.[4] The maculopathy usually is reversible after the drug is stopped.[5] Alpha-adrenergic agonists and topical carbonic anhydrase inhibitors are also useful as second-line drugs.

Orally administered **carbonic anhydrase inhibitors** are very unpleasant drugs because of their numerous side effects particularly in the elderly. With the advances that we have available today in microsurgical techniques and consequent good results, these drugs play no role in the therapy of chronic glaucoma, particularly in older patients. Oral glycerin or isosorbide (50 cc) may be helpful to rapidly lower IOP.

Argon Laser Trabeculoplasty

The results of ALT in aphakic and pseudophakic eyes is less encouraging than in phakic eyes with a success rate of approximately 50%.[6] When it works the pressure-lowering effects are sustained after uncomplicated cataract extraction with or without an intraocular lens implant. The procedure still can be used with some success in aphakic and pseudophakic eyes if an adequate degree of angle remains open. The results in pseudophakic eyes are somewhat more encouraging, but there have been no extensive studies published.

Indications for Surgery

Filtration procedures for aphakic or pseudophakic eyes should be performed routinely with mitomycin or 5-FU intraoperatively, at surgery or 5-FU post-surgery. The **indications** for surgery in the aphakic or pseudophakic patients with higher than normal IOP with medical therapy and failed ALT are: 1) Eyes with pathologic cupping of the disc and glaucomatous field loss. 2) Eyes with normal

discs and visual fields with intraocular pressures persistently over 25 mm Hg in patients over 60 years of age. There is a high incidence of retinal vein occlusion in patients with increased IOP in this age range. 3) Glaucomatous eyes in which the surgeon considers the **target pressure** is inadequate. 4) Eyes with normal discs and visual fields where surgical intervention is necessary for other reasons, e.g., vitreous strands adherent to the cataract section or corneo-vitreous touch with corneal endothelial decompensation or high postoperative astigmatism.

SECONDARY GLAUCOMA WITH UVEITIS

Uveitis is the second most common underlying disease process leading to Secondary Glaucoma. Complicated cataract surgery is the first most frequent cause.

Mechanism of Secondary Glaucoma from Uveitis

Early Stages

In the early stages of secondary glaucoma from uveitis, the disease is almost invariably associated with an open-angle, and what one is dealing with, therefore, is open-angle glaucoma due to blockage of the trabeculum from inflammatory cells and tissue debris (Fig. 1).

Later Stages

At a later stage of the disease, in most cases, angle closure occurs, which is either secondary to peripheral synechiae (Fig. 1).or secondary to pupil block from inflammatory products in the pupil (Fig. 2). This may also occur initially as a chronic angle closure from peripheral anterior synechiae caused by repeated minor attacks of uveitis, which may go unnoticed.

The important point as you first see the patient is to recognize whether you are dealing with an open or closed angle mechanism, done by adequate gonioscopic evaluation of the angle. Occasionally one may find that the angle appears to be open, but there are scattered peripheral anterior synechiae in the angle. This is still an open angle

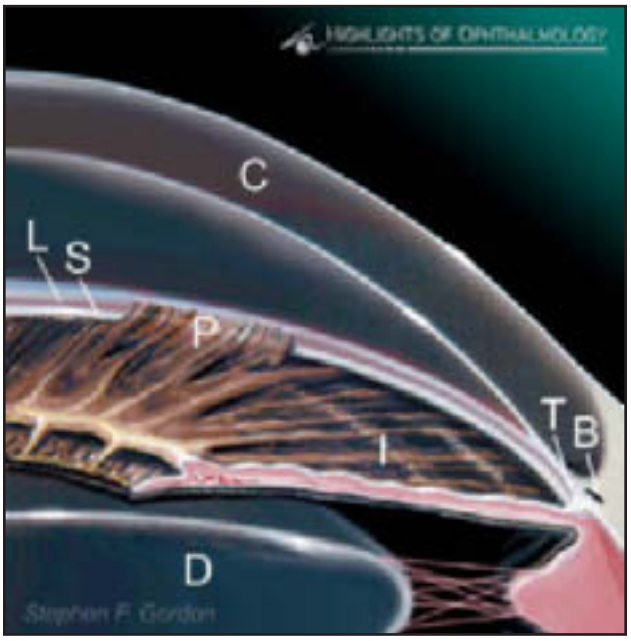


Fig. 1: Predominantly Open Angle with Secondary Glaucoma from Uveitis

In the early stages of secondary glaucoma from uveitis, the disease is mostly associated with an open angle as seen above in this anterior chamber cross section. Blockage of aqueous outflow is due to inflammatory cells and tissue debris in the trabeculum (T). In later stages, peripheral synechiae (P) often occur. An angle is considered predominantly open if less than 50% of the angle is closed by peripheral synechiae. Schwalbe's line (L). Scleral Spur (S). Schlemm's canal (B). Sclera (A). Cornea (C). Iris (I). Lens (D). Treatment predominantly medical.



Fig. 2: Predominantly Closed Angle with Secondary Glaucoma from Uveitis

This cross section of the anterior chamber shows a predominantly closed angle (A) with more than 50% of the angle closed. These later stages of angle closure may be from peripheral synechiae or secondary to pupil block from inflammatory products in the pupil (P). Lens (L). Cornea (C). Notice that the angle anatomy cannot be seen with gonioscopic examination due to the anterior displacement of the peripheral iris (large arrow).

(Fig. 1). If the angle is predominantly open, one regards this and treats it as open-angle glaucoma. If the angle is predominantly closed —and by that one means that more than 50% of the angle is closed by peripheral synechiae—then, one regards this and treats it essentially as an angle closure type of glaucoma (Fig. 2).

If the angle is open, controlling the uveitis will control the intraocular pressure unless the condition has continued for some time and there are permanent fibrotic changes in the trabeculum, in which case the secondary glaucoma will remain as a permanent feature. In some of these cases, after a long period of uncontrolled uveitis, the angle will slowly close in a chronic fashion by peripheral anterior synechiae (Fig. 2). In these cases, of course, the glaucoma will also remain as a permanent feature.

Regimen for Control of Secondary Open Angle Glaucoma With Uveitis

The significant aspects of management of these cases are outlined in Fig. 3. The flow chart shown in Fig. 3 presents the management recommended by **Luntz**. Medical treatment is emphasized initially because once the uveitis has resolved, the glaucoma will also resolve unless there has already been widespread trabecular fibrosis or chronic angle closure. The medical treatment follows a standard pattern. First, mydriatics to dilate the pupil and to put the uveal tissue at rest. An important point in mydriatic treatment is to avoid cyclopentolate, because this topical medication has a pharmacological,

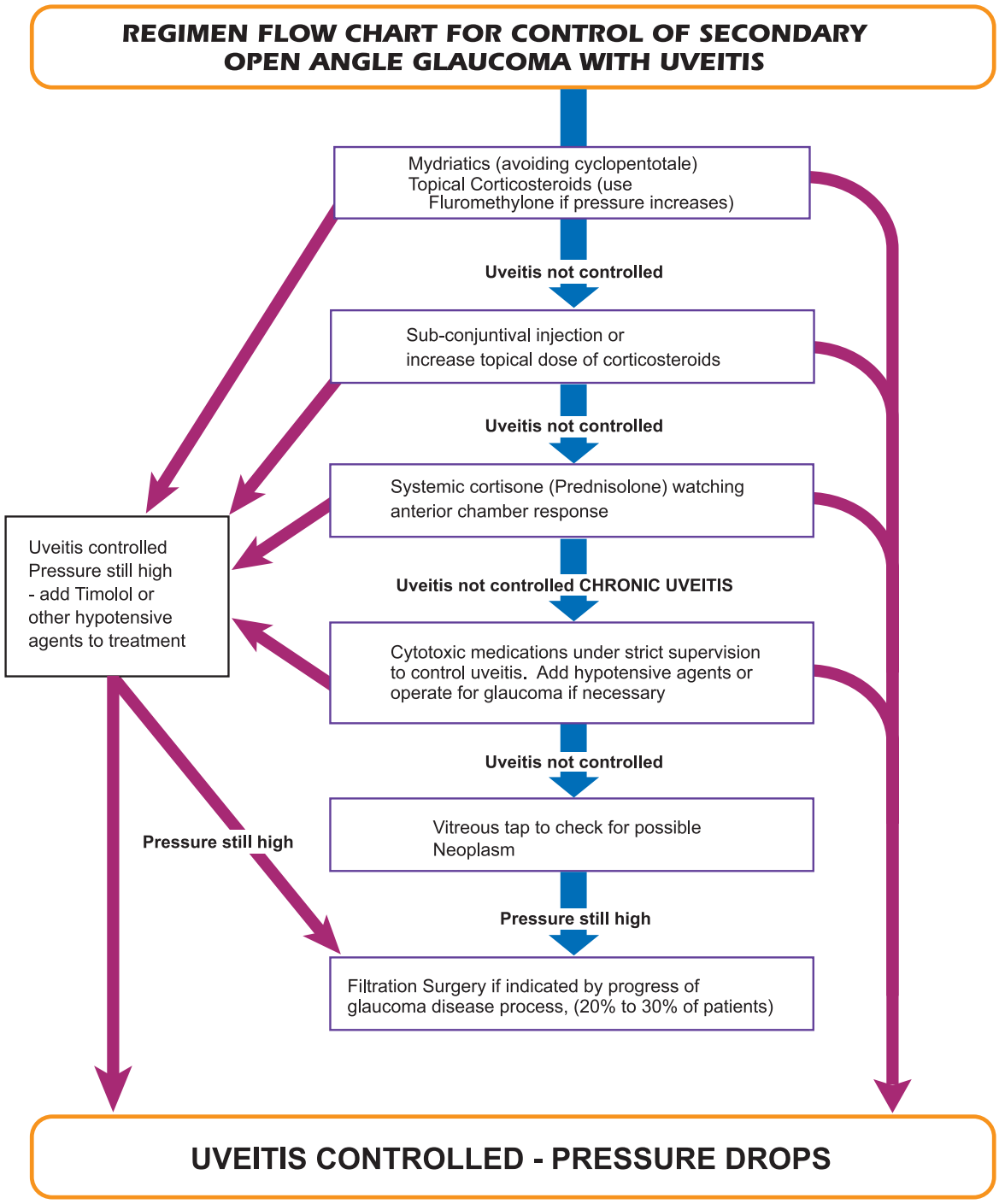


Fig. 3: Regimen Flow Chart for Control of Secondary Open Angle Glaucoma with Uveitis

This flow chart outlines the approach to treatment of patients with open angle secondary glaucoma with uveitis. The sequence of treatment begins at the top of the chart and terminates in the bottom.

pressure elevating effect on the eye in approximately 10% of normal individuals.

Topical Corticosteroids

The second form of treatment is the use of topical corticosteroids (Fig. 4). This has some problems because in 20% - 30% of individuals[7] they will produce a rise of intraocular pressure. If this does occur, one should switch to Fluoromethylone or similar steroids, which have less of a pressure-increasing effect but are also weaker anti-inflammatory agents.

Subconjunctival or Sub-Tenon's Injections

In patients who do not respond to mydriatics and topical corticosteroids one can consider the use of subconjunctival injections of steroids (Fig. 4), but in Luntz' view, one does not get a better response to the steroid by subconjunctival injections as opposed to the more frequent use of topical instillation of the steroid. He prefers, in unresponsive cases, to increase the topical application of steroids from 4-times a day to every two hours or even every hour. This will generally give the same response as a subconjunctival injection. Steroid theraphy should not be used for prolonged periods as steroids may cause steroid - induced cataract[8] or increased IOP.[7-9]

Negative Aspects to Sub-Tenon's Injections

Subconjunctival injections have serious disadvantages. They are painful and irritating. They also produce fibrosis of the conjunctiva, and if it becomes necessary to intervene surgically at a later time, conjunctival fibrosis can be a serious handicap.

Systemic Steroids Monitored by Anterior Chamber Response

In those patients who still do not respond adequately in terms of an anti-inflammatory effect, one has to resort to the use of systemic steroids (Fig. 4). Luntz prefers to use prednisolone orally in doses of up to 120mg a day, monitored by the anterior chamber reaction. By this he means that we start the patient on a high dose — and he starts off with 120mg daily — and if the exudate in the anterior chamber reduces its level of activity, then he reduces the amount of steroid, watching the activity in the anterior chamber. If the activity in the anterior chamber increases at a particular level of systemic corticosteroid, then he increases it slightly and waits until the anterior chamber response settles, and then again reduces the steroid, always watching the anterior chamber response.

The Role of Cyclosporin – A

How do we manage the patient with glaucoma secondary to chronic uveitis, where medical treatment with mydriatics and steroids does not work? **Luntz** divides the subject into those patients who are not responding to the anti-inflammatory medications in terms of the inflammatory response and have a high intraocular pressure and those that have responded in terms of the inflammatory response, but still have a high intraocular pressure. The first group of patients are really refractory-uveitis patients. One has to, at this point, **consider the use of cytotoxic medications such as cyclosporin - A**[10] or Methotrexate[11] under strict supervision. These medications need to be used with caution, but are extremely useful in refractory-uveitis cases.

In the majority of patients with severe uveitis and secondary glaucoma, control of the uveitis will control the glaucoma. This is the primary approach to therapy. If the angle is open and the uveitis is refractory, all possible means should be used to control the uveitis, as in many of these patients the glaucoma will come under control.

Indications for Surgery

Surgery becomes necessary in **secondary glaucoma from uveitis** if the medical regimen that we have discussed does not maintain the intraocular pressure at acceptable levels for a prudent period of

time. These levels may vary from one ophthalmologist to another. **Luntz** thinks a reasonable approach is to accept levels of pressure between 35 to 40mm Hg if the optic nerve head is normal, for one to two months, watching the optic nerve head. Provided there is no increase in the cup-to-disc ratio and provided there is no increase in pallor of the optic nerve head, and normal visual fields, then he believes that one is reasonably safe to continue medication if the uveitis is still active and the ophthalmologist believes there is a chance that the intraocular pressure may still improve with a reduced activity of the uveitis. If the optic nerve head, however, is already showing signs of damage or there are changes in the visual field which are specific for glaucoma , then it becomes urgent to intervene surgi-cally, as soon as the uveitis is as best controlled as one can get it. In general terms, 20-30% of patients with secondary glaucoma from uveitis will require surgery (Fig. 4).

When extensive peripheral anterior synechiae and angle damage have occurred, a trabeculectomy with antimetabolites is necessary. Seclusio pupillae can be abolished simply by peripheral iridectomy (surgical or laser) if the iris plane is anteriorly bowed. Peripheral iridectomy and dissecting free the pupil (Fig. 6) or sector iridectomy is necessary if there is very extensive iris-lens adhesion.

Testing for Intraocular Neoplasms in Secondary Glaucoma With Refractory Uveitis

In every case of refractory uveitis, particularly if the intraocular pressure remains at very high levels (higher than 35mm Hg) for 6 weeks or more one must consider the possibility of an intraocular neoplasm, particularly reticulum cell sarcoma or lymphoma before undertaking glaucoma surgery. These patients should have a vitreous and aqueous tap performed (Fig. 4) and the specimen of aqueous and vitreous sent to a pathological laboratory to examine these specimens for the possible presence of malignant cells floating in the fluid (Fig. 3). If malignant cells are found then one is dealing with a neoplasm and not with uveitis

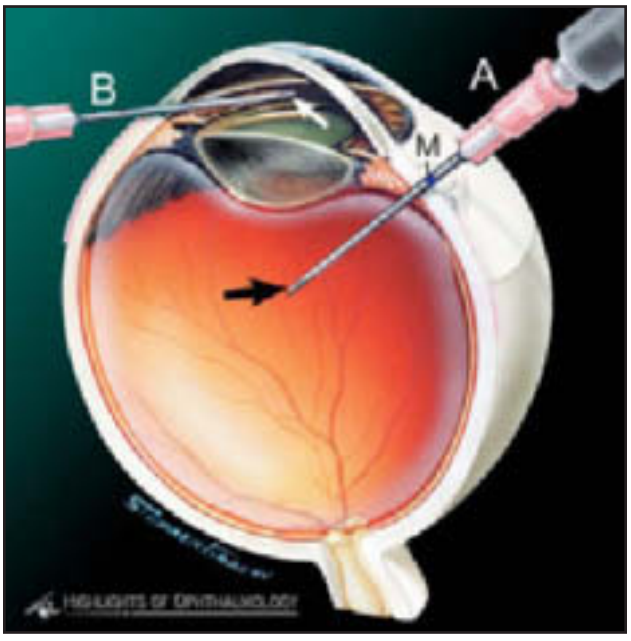


Fig. 4: Testing for Intraocular Neoplasm in Secondary Glaucoma with Refractory Uveitis

If the intraocular pressure remains at very high levels (> 35 mmHg) for six weeks or more, one must consider the possibility of an intraocular neoplasm. A 25 gauge needle (A) attached to a 2cc syringe is inserted through the pars plana at a point 3.5mm posterior to the limbus, toward the center of the globe. A vitreous sample is then aspirated (black arrow). The needle penetrates to a depth of 10 mm as indicated by a mark (M) preplaced on the needle at a point 10 mm from the tip. Separately, an aqueous sample from the anterior chamber is taken (white arrow) with the needle (B) inserted through a paracentesis at the corneo-scleral limbus. If malignant cells are found, then one is dealing with a neoplasm.

ACUTE SECONDARY ANGLE CLOSURE GLAUCOMA FROM UVEITIS

This disease is invariably caused by a pupil block mechanism. The usual cause of the pupil block is an accumulation of exudates from the uveitic process or fibrosis and the formation of posterior synechiae in the pupil. These are patients in whom mydriatic treatment has not adequately prevented the pupil block (Fig. 5).

Patients that have pupil block with iris bombe and secondary closure of the angle and high pressure, constitute a surgical emergency (Fig. 5). If the pupil block is not relieved medically within 72 hours, then one should intervene surgically (Fig. 6).

Laser Iridectomy vs Surgical Iridectomy in Uveitic Eyes

There are two methods of approach. One is by using the laser and performing a laser iridectomy. Laser surgery is very useful if the uveitic process is under control or reasonably well controlled; but **in an eye with active uveitis** the laser is less effective and may cause corneal burns or lens opacity. In these cases, a surgical iridectomy is preferable.

Luntz uses the same laser settings that are employed for laser iridectomy in non-uveitic eyes. However, in eyes with uveitis the cornea is not as tolerant to laser surgery as in non-uveitic glaucomatous eyes, possibly because of the involvement of corneal endothelium in the uveitic process. Corneal epithelial or endothelial burns are seen after fewer laser applications than in non-uveitic eyes. As soon as this is noted, the procedure should be stopped. It can be repeated at a later date. But upon observing this, it means that we cannot use as much power or as many burns at the initial sitting in that eye as one can in laser iridectomy for non-uveitic eyes and it may require more than one session of laser surgery to fashion an iridectomy. This is a disadvantage if there is pupil block with high intraocular pressure.

Luntz' own approach is that, if at the first sitting, he cannot make an opening in the iris by laser iridectomy before developing corneal burns, he will immediately take the patient to the operating room and perform a surgical iridectomy. This has become rarely necessary since the advent of Nd:YAG laser iridectomy.

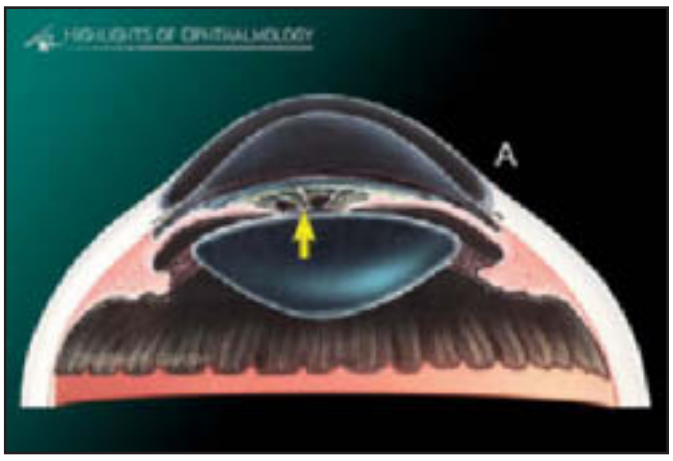


Fig. 5: Mechanism of Acute Secondary Angle-Closure Glaucoma Caused by Pupillary Block - Cross Section View

The pupil block is caused by exudates from the uveitic process or fibrosis and the formation of posterior synechiae in the pupil (arrow). Aqueous accumulates in the posterior chamber, the iris is pushed forward. Patients with pupil block with iris bombe and secondary closure of the angle (A) and high pressure constitute a surgical emergency.

The Pupil Bound Down With Posterior Synechiae

If the pupil is so small and bound down with posterior synechiae that the patient will not have good vision through that pupil following a laser iridectomy, then one has to liberate the pupil (Fig. 6). The technique to release synechiae using viscoelastics as shown in Fig. 6) is much less traumatic than the previously used method using an iris spatula

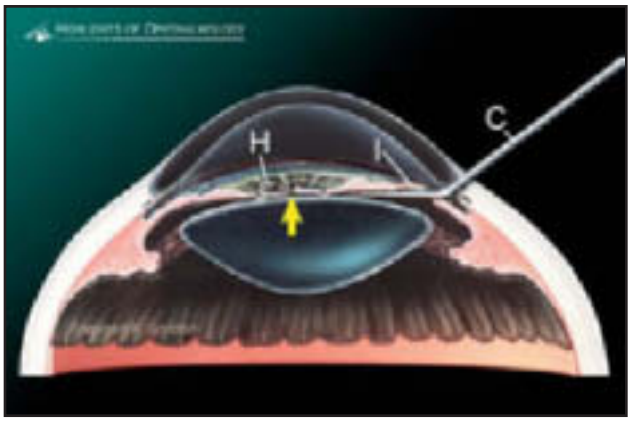


Fig. 6: Surgical Release of Pupil Synechiae in Secondary Glaucoma -Cross Section View

A cannula (C) attached to a So-dium Hyaluronate syringe is inserted into the anterior chamber through a paracente-sis in the cornea adjacent to a peripheral iridectomy. The cannula is advanced through the iridectomy (I) and under the iris to a site adjacent to the anterior synechiae (arrow) which are to be rup-tured. Sodium Hyaluronate (H) is injected under the iris, resulting in ballooning of the iris and tension on the iris at the site of the synechiae. This is usually sufficient to break the synechiae. However, if the synechiae are firmly adherent by fibrous tissue, mechanical rupture of the synechiae using the Sodium Hyaluronate cannula may be necessary, in addition to stretching of the iris with Sodium Hyaluronate. Multiple posterior synechiae are ruptured individually in this fashion. If peripheral iridectomy is not present, the cannula can be advanced under the iris through the pupil at a site close to the peripheral synechiae, then proceeding in the same manner.

ACUTE SECONDARY ANGLE CLOSURE GLAUCOMA FROM INTUMESCENT CATARACT

In some instances one is faced with a patient who has an intumescent mature or hypermature cataract which has produced uveitis plus pupil block, both from the uveitic process and from the large lens. When the uveitis subsides, the angle remains very narrow or closed because of the large lens, and the patient has intermittent bouts of raised pressure or even continuously raised pressure.

In these cases it is necessary not only to control the uveitis, but also to remove the cataract. If the pressure is reduced by anti-inflammatory treatment and mydriasis, then the cataract can be removed using a standard cataract extraction technique. However, if the pressure remains high and does not respond to treatment with topical and/or systemic hypotensive agents then a posterior sclerotomy is done at the time of surgery removing fluid from the vitreous body. This is a safe way to reduce the intraocular pressure, and then proceed to remove the cataract.

SECONDARY MALIGNANT GLAUCOMA

This is a secondary glaucoma which most often occurs following invasive surgery for angle closure glaucoma and also cataract surgery. It is characterized by a flat or very shallow anterior chamber with a higher than average intraocular pressure at some time during the course of the disease. The pressure does not respond to topical hypotensive medications (miotics, B-blockers, adrenergic agent, prostaglandins) or to classical filtering glaucoma surgery, but in many cases it will respond to topical cycloplegics. In some instances the onset of malignant glaucoma can be delayed many years following glaucoma surgery.

Luntz and **Rosenblatt** [12] describe this disease as characterized by a blockage to normal aqueous flow and an abnormal accumulation of aqueous in the posterior chamber, vitreous and/or supra-choroidal space and they will all respond, if medical treatment has failed, to surgical management based on the principles of: 1) Identifying the site of blockage and aqueous accumulation; 2) Relieving the block either medically or surgically; 3) Draining the accumulated aqueous.

Specific measures for management is illustrated in Fig. 7. **Luntz** and **Rosenblatt**[12] also believe that malignant glaucoma encompasses a number of different mechanisms that should each be recognized — for example, secondary pupil block, ciliary lens block (Fig. 7) ciliary-vitreal block (Fig. 8) and irido-lens block. Aqueous accumulates in the posterior chamber (Fig. 6). Such precise localization of the pathology facilitates appropriate medical therapy and appropriate surgical management.

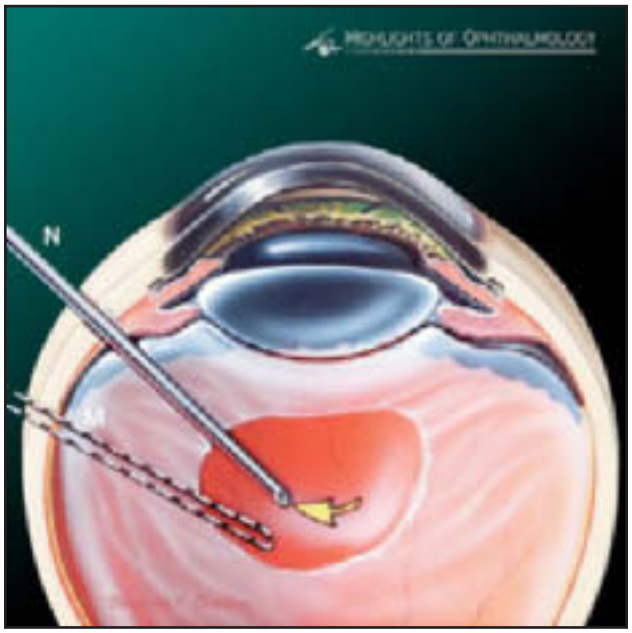


Fig. 7: Surgical Treatment of Ciliary and Irido-Lens Block (Malignant Glaucoma)

Aspiration of the aqueous fluid (arrow) from the vitreous cavity is performed with a 20-gauge needle (N), inserted through a posterior sclerotomy 3 mm from the limbus. Note the displaced anterior chamber structures. The iris and ciliary body are pushed forward, the posterior chamber is obliterated. A posterior sclerotomy placed beyond 4-5 mm from the limbus results in the needle (M) penetrating the vitreous base. Because the vitreous is adherent to the pars plana in this area, the needle may not penetrate the anterior hyaloid here. This is followed by peripheral iridectomy and aspiration of the aqueous fluid previously trapped in the vitreous. The anterior chamber structures return to a more normal position when the posterior pressure source is alleviated or removed. The anterior chamber is filled with viscoelastic.

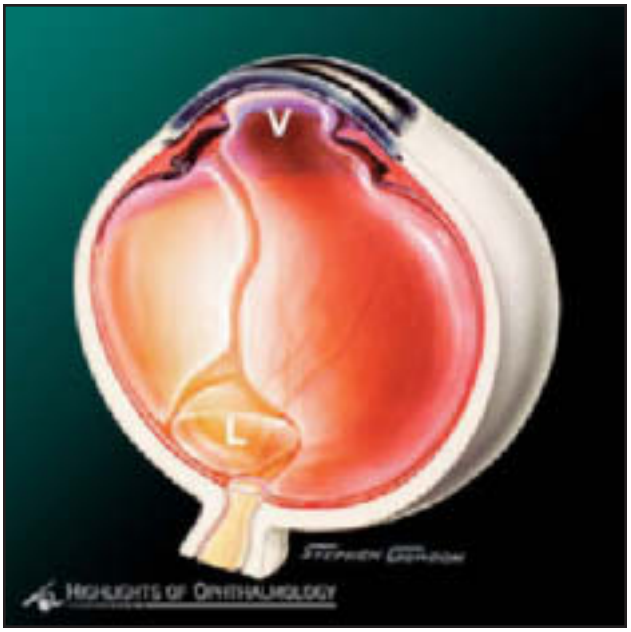


Fig. 8: Totally Dislocated Lens. Mechanism of Secondary Glaucoma from Irido Vitreous-Block

This cross sectional view shows the totally dislocated lens or lens nucleus (L) with vitreous (V) in the anterior chamber and the iris diaphragm pushed anteriorly obliterating the anterior chamber and causing pupillary block glaucoma. As advised by Malbran, such a case is a candidate for a vitrectomy accompanied by the use of perfluorocarbon liquid to float and lift the nucleus from the vitreous cavity and easily remove it without touching the retina. The vitreous is carefully cleaned from the wound and anterior chamber and a trabeculectomy is performed. (See Figure 9 for modern vitreoretinal technique for removal of dislocated lens in the vitreous using perfluorocarbon liquid - **Editor**).

Management of Malignant Glaucoma

Pre-Ciliary Block or Pre-Malignant Syndrome

"Malignant glaucoma" is unresponsive to traditional filtering glaucoma surgery. Surgical treatment is aimed at relieving the pupil or ciliary body block and draining fluid aqueous accumulation either from the posterior chamber (by laser or surgical peripheral iridectomy) or from the vitreous by aspirating the aqueous pocket through a posterior sclerotomy, or from the suprachoroidal space also through a posterior sclerotomy incision (Fig. 7). A preferable surgical technique for removal of aqueous pocket in the vitreous is by formal vitrectomy. Occasionally it may be impossible to differentiate the actual causal mechanism, or **more than one mechanism may be implicated**, and the surgeon should be prepared to treat all possibilities.

Luntz recommends initial medical treatment with Cyclopentolate hydrochloride 1% administered every 10 minutes for 2 hours and then qid, carbonic anhydrase inhibitor 250 mg four times a day given concurrently, as well as a steroid drop four times a day. After 24 hours, if there is no response, the cycloplegic therapy is discontinued and the patient is given 75 cc of glycerol 50% bid orally flavored with fruit juice and over ice cubes together with steroid drops topically qid. This regimen is usually successful.[13] It may be repeated for another 24 hours if the **anterior chamber has not reformed, provided there is no corneal stromal edema, there has been no physical lens-cornea contact, and the intraocular pressure is not too high**. When these circumstances are present at the onset, oral glycerol therapy is instituted without delay. Cataract will rapidly develop unless the anterior chamber is promptly reformed. In **Luntz'** view, immediate surgical intervention is necessary if the endothelial surface of the central cornea remains in actual contact with the lens capsule for more than 24 hours.

Secondary pupil block due to organized adhesions between the pupil margin and anterior lens capsule or vitreous face (aphakic eye) may result in the accumulation of aqueous in the posterior chamber and increased pressure in the posterior chamber. The iris is anteriorly bowed (bombe) and pushed onto the posterior corneal surface flattening the anterior chamber. It may drag the lens with it if there is synechial attachment to the pupil margin. The angle closes and the intraocular pressure rises (Fig. 7). Miotics may aggravate the situation and are best avoided. The non-expected sequence of events following instillation of pilocarpine which may contribute to ciliary block glaucoma, will not exist in the presence of an iridectomy unless the coloboma is blocked and fails to communicate with the mass of fluid trapped in the posterior chamber. At the present time, the laser makes surgical entry into the eye unnecessary.

Ciliary and/or Irido-Lens Block and Irido-Vitreous Block

A more intensive form of pupil block occurs when the iris is adherent to the anterior lens capsule. The posterior chamber is obliterated and aqueous drains into the vitreous, forming a vitreous pocket, increasing vitreous pressure and pushing the lens-iris diaphragm anteriorly (Fig. 7) resulting in a flat anterior chamber with raised intraocular pressure. However, as the posterior chamber is obliterated the iris surface is flat and not convex, as in pupil block. This is an important clinical differentiating point.[14] In pupil block with an expanded posterior chamber, laser iridectomy is the treatment of choice. In irido-lenticular block the posterior chamber is obliterated and laser iridectomy could be dangerous. In these eyes iridectomy, posterior sclerotomy and removal of trapped aqueous from the vitreous is necessary preferably by formal vitrectomy.[13] (Fig. 7). When there is irido-vitreous block (Fig. 8) we must proceed as described in Figs. 8 - 9.

Engorgement and anterior rotation of the ciliary body may result in ciliary processes moving anteriorly and centrally and contacting the lens equator or hyaloid face. Aqueous flow through the zonules is obstructed and pockets of aqueous accumulate posteriorly. **Shaffer** and **Hoskins**[15] named this condition "ciliary block" glaucoma. Ciliary block is only one of many mechanisms which cause the clinical entity of malignant glaucoma. Ciliary block is undoubtedly a primary factor in the etiology of some and probably in most cases of malignant glaucoma, while in others it appears to play very little or no part as an etiological factor. Management of these entities is shown in Fig. 7

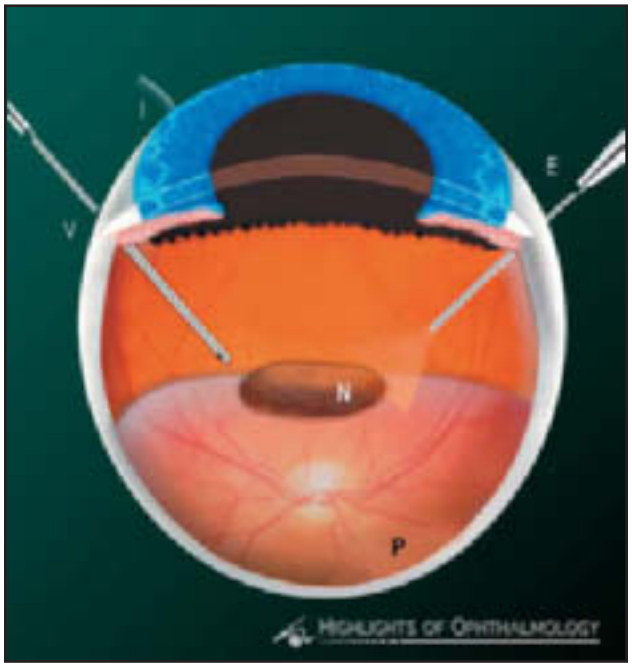


Fig. 9: Perfluorocarbon Liquid used in Luxated Crystalline Lens Fragments.

Fragmentation (V) of nucleus particles (N) can be performed on a cushion of PFCL (P), since the perfluorocarbon liquid acts as a shock absorber for the ultrasonic energy. In these cases, to avoid crisis of intraocular pressure it is recommended to perform a complete vitrectomy and removal of every single fragment of nucleus from the dislocated crystalline lens. The vitreous cavity may be left filled with balanced salt solution in a non-complicated case. Infusion canula (I).

SECONDARY GLAUCOMA FROM BLUNT TRAUMA

The usual causes of secondary glaucoma following blunt or non-penetrating trauma are related to blockage of the trabecular meshwork with blood or its degradation products (Fig. 10) or with inflammatory debris from uveitis in the presence of an open angle. Other causes may also play a part, such as displacement or sub-luxation or dislocation of the lens into the anterior chamber; or, if the lens is ruptured, obstruction to the trabeculum by lens protein (phacolytic glaucoma). Following glaucoma secondary to complicated cataract extraction and glaucoma secondary to uveitis, blunt trauma is the third most frequent cause of secondary glaucoma.[16]

Ghost-Cell Glaucoma

An interesting but rather less common type of secondary glaucoma from blunt trauma which occurs much later is the "ghost-cell" glaucoma in eyes that have suffered a contusion injury followed by vitreous hemorrhage.

The vitreous hemorrhage absorbs, but not totally, leaving behind the membranes of red cells (ghost-cells) or degenerated red cells in the anterior vitreous (Fig.10). The anterior chamber and anterior vitreous contain cellular debris and pigmented cells (Fig. 10). These cellular products gradually

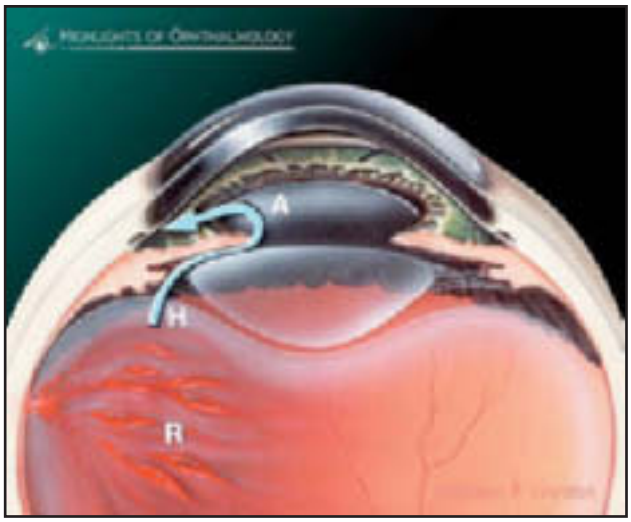


Fig. 10: Mechanism and Management of Ghost Cell Glaucoma

In eyes with contusion injury and vitreous hemorrhage (R), cellular products may migrate (arrows) through a trauma-induced rupture of the hyaloid face (H) into the anterior chamber (A), obstructing the trabeculum and causing late secondary open angle glaucoma. This situation is treated by washing out the cellular debris from the anterior chamber via a paracentesis. If this does not control the glaucoma, a trabeculectomy with or without antimetabolites is performed.

migrate through a trauma-induced rupture of the hyaloid face into the anterior chamber and then, at a later stage, obstruct the trabecular meshwork, causing a late, secondary open-angle glaucoma.[17] (Fig. 10). This "ghost-cell glaucoma" is treated by paracentesis and anterior chamber washout of the cellular debris. If this does not control the glaucoma, then a trabeculectomy with or without antimetabolites (depending on the severity of the case) is performed. If this is unsuccessful, vitrectomy is the next step.

Angle Recession Glaucoma

A second mechanism for glaucoma in a contusion injury is angle recession glaucoma. This is the result of significant damage to the anterior chamber angle (Fig. 11). In less severe injuries the fibers of the ciliary body are split apart. When trauma is extensive it may result in different degrees of dislocation of the ciliary body from the scleral spur (Fig. 11) leading to fibrosis of the trabecular meshwork.[18] Gonioscopically the ciliary body band, which is normally attached to the scleral spur, is torn from the scleral spur and a band of white sclera is visible between the ciliary body and the scleral spur (Fig. 11).

Both secondary open-angle glaucoma from hyphema and secondary open-angle glaucoma related to angle recession may, in later stages, develop peripheral anterior synechiae and secondary angle-closure glaucoma. The treatment of secondary glaucoma from trauma will depend on the mechanism whether the glaucoma is open-angle or angle-closure and if hyphema is present or absent.

Treatment of Angle Recession Glaucoma

Angle recession glaucoma may be present within a few weeks after a severe blunt injury resulting in edema of the trabecular meshwork. If the injury is not quite so severe but there is angle recession, the glaucoma may occur much later due to over-growth of the endothelial cells from the cornea into the angle covering and obstructing the trabecular meshwork (Fig. 11); alternatively, peripheral anterior synechiae form in the angle resulting in angle closure glaucoma .

The management approach to angle recession glaucoma, if the angle is open, is by argon laser trabeculoplasty in the first instance. If the laser treatment fails, the next step is to do a filtering operation choosing trabeculectomy with antimetabolites.

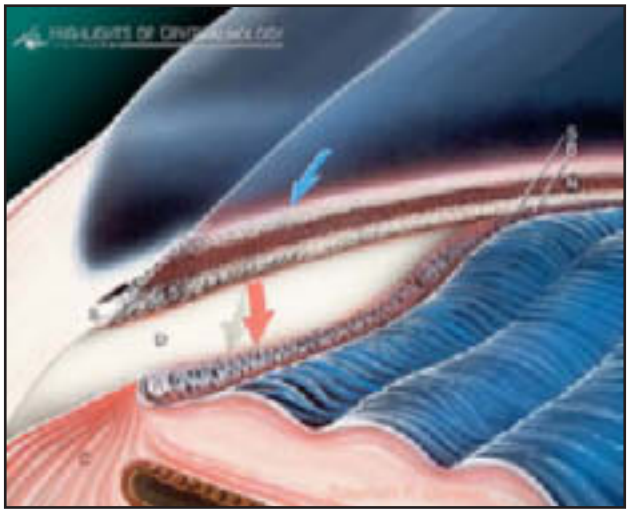
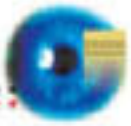


Fig. 11: Mechanism of Angle Recession Glaucoma

In less severe contusion injuries the fibers of the ciliary body are split apart. More severe blunt trauma results in actual dislocation (black arrow) of the ciliary body (C) from the scleral spur (S). In this cross section of a gonioscopic view, the white sclera (D) is visible between the ciliary band (B) and the scleral spur (S). The ciliary band (B) is normally attached to the scleral spur (normal configuration is shown at N). Overgrowth of the endothelial cells or endothelialization from the cornea (white arrow) into the angle covering and obstructing the trabecular meshwork in this area of angle recession can occur causing glaucoma with an open angle at a later date.



Angle recession glaucoma has a high incidence of failure with standard filtering surgery without antimetabolites.

Management of Traumatic Secondary Glaucoma and Hyphema

The treatment of traumatic hyphema is somewhat controversial. Usually the patient is allowed to be ambulatory. Only the traumatized eye is patched. Pilocarpine 2% may be used four times a day together with a mydriatic, usually neosynephrine 2.5% four times a day, in order to maintain mobility of the pupil. Topical prednisolone acetate 1% is most important, as many of these eyes also have uveitis. Other glaucoma medications such as topical carbonic anhydrase inhibitors, alpha agonists and prostaglandins may be effective but beta-blockers are not of much use in these particular patients. The use of e- aminocaproic acid is controversial,[19] dose suggested is 50mgm/kg every 4 hours.

A careful watch is kept on the intraocular pressure and for corneal blood staining. If after the first 48 hours intraocular pressure is **quite high** in spite of medical therapy and the cornea begins to show evidence of damage, then a paracentesis is indicated without delay to evacuate the hyphema. Usually this is easily done unless the blood has clotted in the anterior chamber. If this is the case, we may inject 0.3cc of streptokinase into the blood clot, using an Ocutome cutting and suction instrument. It is important not to do any lavage or surgery within the anterior chamber until the tissue structures are visible. Fibrinolytic agents have been used on and off during several years.[20] The results with their use is not conclusive.

If this is not effective in controlling the glaucoma, the same principles as previously outlined for the surgical management of glaucoma are followed, depending on whether the secondary glaucoma is related to an open-angle or chronic angle closure.

If the cornea is not affected and the pressure is only moderately high, it is preferable to wait and keep the patient under aggressive medical therapy before proceeding with surgery.

On the seventh day, if there has been a repeat bleeding, the eye is painful and the progress is unsatisfactory, a lavage of the anterior chamber may be done with extreme care.

Ultrasound studies are indispensable to determine whether there is any posterior damage to the globe. I is also prudent to check for sickle cell disease. These patients require more aggressive treatment.

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Chapter 40
GLAUCOMA RESULTING FROM VITREORETINAL PROCEDURES

Lihteh Wu, M.D.

Transient or sustained elevation of intraocular pressure (IOP) is a frequent complication following vitreo-retinal procedures, produced by a variety of mechanisms. Primary and secondary glaucoma of both closed and open angle types may occur. To accurately detect an elevated IOP, applanation tonometry is recommended. Schiotz indentation tonometry gives falsely low values in eyes with a scleral buckle and is notoriously inaccurate in eyes with an intraocular gas bubble. Sometimes the corneal epithelium must be removed intraoperatively to improve visualization. On the first few post-operative days, Goldman applanation tonometry can't be accurately performed in these eyes. The Tono-Pen is the recommended instrument although one must keep in mind that the Tono-Pen underestimates the true IOP by about 10 mm Hg in eyes with an IOP greater than 30 mmHg.

Scleral Buckling

Secondary angle closure glaucoma is seen in up to 7% of scleral buckle cases. Risk factors include a large encircling buckle anterior to the equator, elderly patients and damage to the vortex veins which leads to problems with venous drainage. Under these circumstances a serous choroidal detachment occurs. This leads to anterior rotation of the ciliary body with a concomittant displacement of the peripheral iris into the anterior chamber angle. The peripheral iris may also be pushed forward in the absence of choroidal detachments if a high encircling buckle displaces the crystalline lens anteriorly. The prognosis is favorable and spontaneous resolution usually occurs once the choroidal detachment resolves 2-3 weeks post-operatively. The elevated IOP is controlled medically in most cases. Rarely, severe flattening of the anterior chamber mandates surgical drainage of the choroidal detachments. Laser iridotomy followed by laser iridoplasty may be tried to open up the angle. The recommended laser settings for iridoplasty includes a spot size of 200 µm, duration of 0.2 sec and 1.3 – 1.5 mj power.

Pars Plana Vitrectomy

During pars plana vitrectomy, the endothelial cells lining the trabecular meshwork may be damaged by the irrigating intraocular solution, post-operative inflammation (especially when extensive cryotherapy or photocoagulation are performed) and steroid susceptibility resulting in raised intraocular pressure. This is usually manifested in the first 48 hours following surgery (Fig. 1). Fortunately this damage is usually mild and controlled with the usual anti-glaucoma medications.



Fig. 1: Temporary Intraocular Elevation Secondary to Retinal Photocoagulation

Postoperative inflammation secondary to laser treatment (cryotherapy, argon laser photocoagulation or Nd: Yag laser treatment) may result in temporary elevation of intraocular pressure. This manifestation is present in the first 48 hours following surgery and fortunately is usually mild and controlled with anti-glaucoma medications.

The trabecular outflow channels may be obstructed by red blood cells. This usually occurs in diabetic aphakic eyes. Most cases can be treated with anti-glaucoma medications until the hemorrhage clears. In the few cases that are refractory to medical treatment, lavage of the vitreous cavity is usually curative.

Intraocular Gases

Intraocular gases have become an useful adjunt in vitreoretinal surgery. Practically all of the intraocular gases currently used in vitreoretinal surgery, with the exception of air, have expansile properties. When a pure gas is injected into the vitreous cavity it will expand. Oxygen, carbon dioxide and nitrogen, among other gases, are present in the surrounding tissue fluid. These gases diffuse into the injected gas bubble expanding it until the partial pressures between the two compartments become equal. The time of maximal gas expansion is 6 to 8 hours after injection. For instance, SF6 expands to twice its volume and 50% of this expansion occurs within 6 hours. C3F8 expands to four times its volume. This rapid expansion will increase the IOP despite an open angle if sufficient fluid can't be displaced from the eye to accommodate the expanding gas volume. For the most part, anti-glaucoma medications usually suffice. If the IOP is still elevated, a small amount of intraocular gas is removed with a 30 gauge needle (Fig. 2). If the intraocular bubble is large enough, it may displace the lens and iris anteriorly causing secondary angle closure glaucoma. If the patient is aphakic or pseudo-phakic a smaller bubble may cause pupillary block if the patient lies supine. To prevent this, the patient is instructed to lie in a face down position to keep the gas bubble away from the pupillary space.

Rapid expansion of an air bubble occurs during air travel. The IOP rises quickly to dangerous levels as the gas bubble expands. The degree of expansion is a function of the size of the gas bubble. If the patient has a bubble larger than 20%, prophylactic medical treatment will not prevent a rise in the IOP since the expansion of the bubble will overwhelm all the compensatory mechanisms. Patients are allowed to fly when the bubble occupies 20% or less of the vitreous cavity. The eye may be treated with topical and systemic medications prophylactically.

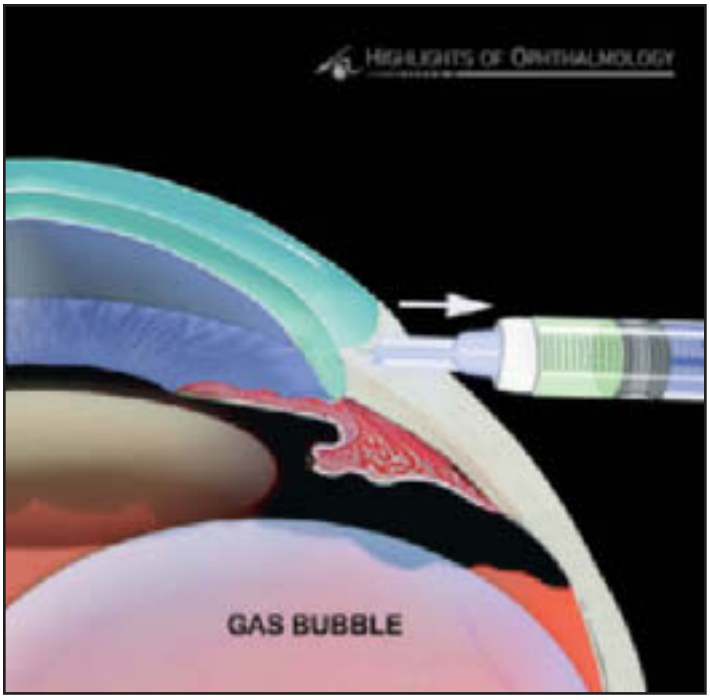


Fig. 2. : Effects of Intraocular Gases on Intraocular Pressure

Intraocular gases currently used in vitreoretinal surgery have expansile properties. This rapid expansion will increase the IOP despite an open angle if sufficient fluid can not be displaced from the eye to accommodate the expanding gas volume. If the IOP is still elevated a small amount of fluid is removed with a 27 – 30 gauge needle through the anterior chamber (arrow).

Silicone Oil

Just like the intraocular gases, silicone oil is part of the growing armamentarium of vitreoretinal surgeons. Glaucoma is a frequent complication of pars plana vitrectomy with silicone oil injection and has been reported in up to 15% of cases. Glaucoma results from the migration of the silicone oil into the anterior chamber. Once in the anterior chamber silicone oil can directly damage the trabecular meshwork or cause peripheral anterior synechiae. In aphakic eyes pupillary block may occur if an inferior iridectomy is not present (Fig. 3). Given enough time, most authorities believe that all eyes with silicone oil will eventually develop emulsification. When emulsification occurs tiny oil droplets gain access to the anterior segment despite the fact that the bulk of the silicone



Fig. 3 (right): Effects of Intraocular Silicone Oil on Intraocular Pressure. Importance of Peripheral Iridectomy.

Silicone oil, another material used in vitreoretinal surgery, may have important effects on the trabecular meshwork. The rise of intraocular pressure may result from the migration of silicone oil into the anterior chamber causing damage to the trabecular meshwork and its structures or peripheral anterior synechiae. Pupillary block may occur if an inferior iridectomy is not present.

remains in the posterior segment. The tiny bubbles may lodge in the trabecular meshwork damaging the endothelial cells. Aggressive medical and surgical management with silicone oil removal, trabeculectomy with mitomycin C, glaucoma shunts, and cyclodestructive procedures shows modest success in controlling IOP.

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Chapter 41
AB-EXTERNO POSTERIOR TRABECULECTOMY FOR SECONDARY AND REFRACTORY GLAUCOMAS

Eduardo Arenas, M.D., F.A.C.S.

Non penetrating Filtering Operations for Glaucoma have increased their popularity during the last few years with the introduction of the ab-externo technique by us ,the collagen implants by Andree Mermoud and the concept of viscocanalostomy by Robert Stegman. We have been performing non-penetrating filtering procedures for the past 25 years with a high level of success and a minimum of complications. - Non penetrating surgical techniques are the ideal surgical procedure for open angle glaucomas, because these techniques incorporate all the anatomical elements, that play an important role in the pathophysiology of the disease. Our success rates are better or similar to other filtering procedures but fewer complications.

When dealing with closed angle glaucomas there are some difficulties with the "nonpenetrating techniques ", mostly because these cases generally have shallows chambers and enlarged lenses, with small quantities of aqueous in the anterior chamber and alterations in the anatomical structure of the trabeculum and the Schlemm´s canal. However we think that nonpenetrating techniques are also useful in treating angle closure glaucomas, if we avoid flat chambers during the surgery and in the immediate postoperative period.

To operate on an eye with secondary glaucoma with all the anatomical elements altered and extensive anterior synechias, presence of vitreous in the anterior chamber, aphakia, and sometimes iris rubeosis is difficult. Most of these cases fail or require implant devices or cyclodestructive procedures. For these cases we have developed a new technique called posterior ab-externo trabeculectomy, that gives a good rate of success with a minimum of complications.

This new procedure is based on the concept that non penetrating filtering surgery, works because a perfect level of intraocular pressure is achieved through a microscopic but permanent communication between the anterior chamber and the bleb.

To understand this concept it is important to remember that if the eye produces approximately 4 cc of aqueous humor per day it is necessary to establish the size of the filtration area in order to maintain an equilibrium . If we compare the eye with a soft and elastic container receiving a permanent inflow of liquid and desire to know how big the opening should be to maintain a constant volume it is necessary to apply hydraulic calculations. Introducing all the possible factors and applying the Bernoulli's theorem, the size of the opening in a simulated eye to keep this balance, will be only 100 microns!!. The size of the opening of a regular trabeculectomy could be 2 million times larger! when performing a 2 mm by 1 mm trabeculectomy. This principle is very important to understand, because it explains why the non-penetrating fistulizing techniques can work producing blebs as large as those observed in standard full thickness or guarded trabeculectomies.

Subsequent to this finding we decided to eliminate, in the last seven years, the scleral flap over the filtering zone, trying to facilitate the new outflow and avoid any unnecessary resistance. Schuman et al[1] have demonstrated in enucleated human eyes that elimination of the external wall of the Schlemm's canal with Excimer laser, decreases by approximately one third the outflow resistance. Similar findings were found by Ellingsen[2] and other authors[3,4].

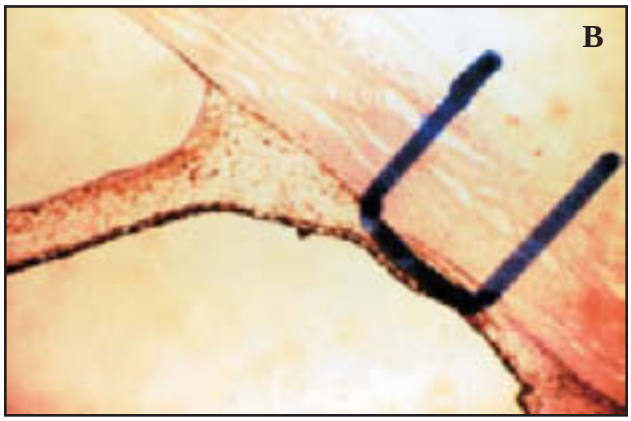
We think that the mechanism of filtration in standard trabeculectomies a few weeks post-surgery depends on the same small size of 100 microns and a balance is reached in the same way as in the non-penetrating surgery. Viewing the surgical area by careful gonioscopy of a successful standard filtering procedure done with any technique, one sees fibrous tissue covering the surgical area and some times a small slit where the aqueous is passing to the bleb. The real point with the non-perforating techniques is to achieve a filtration area with a permanent local pressure high enough to avoid fibrous tissue closing the opening, until new filtration channels are established. When a successful standard trabeculectomy is opened after several years, what we observe is continuous leaking of small quantities of aqueous under the guarded flap of the sclerectomy

Once the aqueous reaches the subconjunctival space it is eliminated in four ways: (1) transconjunctival, (2) by bulk-flow through lymphatic vessels, (3) diffusely through lymphatic vessels or veins (4) throughout new channels. According to Benedict the aqueous veins originate 1 to 2 1/2 mm behind the limbus and join the episcleral veins after a short course. The venous recipients are characterized by a straight and deep course. In eyes with open-angle glaucoma the average number of aqueous veins is found to be increased compared to the number found in healthy eyes

All filtering procedures attempt to form a communication between the anterior chamber and the outer eye or sclera without decompressing the eye.In the last 15 years the implantation of artificial valves (Setons- Editor) placed on the sclera (and into the anterior chamber – **Editor**) have shown a rate of intraocular pressure control , fluctuating between 65 and 85%. In spite of these successes most authors agree that the technique has a high rate of complications. Some end in phthisis bulbi or enucleation.

Histological studies of eye specimens with terminal, secondary and aphakic glaucoma show, that in most of them the root of the iris adheres to the trabeculum narrowing the anterior chamber and increasing the space of the posterior chamber. (Figs. 1 A-B). As part of this process the undergoes





Figs. 1 A-B. Histological Section of the Iris Root in Secondary Glaucomas

This histological studies in terminal, secondary and aphakic glaucomas shows, that in most of them the root of the iris adheres to the trabeculum and ciliary body narrowing the anterior chamber space and deepening of posterior chamber. This process will lead to a progressive shrinkage and atrophy of most of its histological elements and disappearance of the Schlemn´s canal. In B you may observe the area to be treated with the non-penetrating ab-externo filtering technique.

progressive shrinkage and atrophy of most of its histological elements with disappearance of the Schlemn's canal. Another histological change observed in these eyes is progressive shrinkage and atrophy of the ciliary including narrowing and disappearance of the ciliary vessels.

Under these circumstances it is easy to understand why it is so difficult to control the intraocular pressure in eyes with this type of damage. We have obtained good results in these eyes with ab-externo trabeculectomy using a microdiamond drill. In most eyes only a single procedure has been necessary.

Surgical Technique

To decide where the filtrating procedure should be done a detailed gonioscopic pre-surgical analysis is performed to determine the quadrant of the eye in which the posterior chamber is widest. Care should be taken not to choose a fibrotic or cicatricial conjunctival zone. If there are not too many risks, patients are advised to discontinue all the antiglaucomatous medications in order to have a good flow of aqueous during surgery.

1. Under high magnification, 1 cc of 1-% lidocaine hydrochloide is injected subconjunctivally, avoiding as far as possible subconjunctival hemorrhage followed by gentle digital massage. There is no need for retrobulbar or parabulbar blocking because this is an external procedure.

2. Two corneoscleral traction sutures of 7-0 silk are placed at the limbus or in the peripheral cornea, to ensure a permanent and parallel surgical field easy to work with under high magnification.

3. A limbal-based far posterior conjunctival flap is made. It is important to start the incision near the initiation of tarsal conjunctiva, in order to block dissect conjunctiva and Tenon's capsule up to the limbal area.

4. A limbal-based 3 X 1.5-mm rectangular scleral flap of approximately four fifths the scleral thickness is raised.

5. Drilling is started in the deep scleral plane under the scleral flap from one side to the other thinning the scleral bed until flow of aqueous is detected. The drill maneuver continues slowly trying to obtain a meshwork of scleral or uveal tissue until aqueous is seen leaking from the posterior chamber (Fig. 2).

It is extremely important to identify if there is some bleeding associated with the flow of aqueous. Irrigating the wound with saline, makes it possible to observe if there are open vessels that should be carefully cauterized. The identification of a

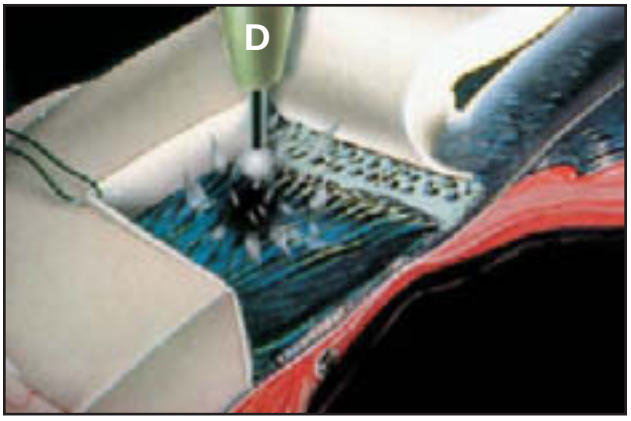


Fig. 2. Anatomical-Surgical view of the Ab-Externo Procedure

This view shows the application of the diamond drill **(D)** over the scleral bed until obtaining an adequate and permanent filtration avoiding a through communication with posterior chamber. The limbal base conjunctival flap allows a better protection and colocation of the mitomicin wet sponge (0.08 mgrs) over 2-3 minutes. This period time must be regulated depending on the age of the patient or the thickness of the conjunctival flap.

permanent flow of aqueous is checked with a Weck cell sponge. When the flow is constant, mitomycin C at a low concentration of 0.08 per cc is placed with a small piece of a Weck cell sponge for 3 minutes.

It is important to remember that the procedure never creates a direct opening through the ciliary body or iris root, therefore mitomycin does not enter the intraocular spaces.

6. If the flow of aqueous humor is adequate and constant, the scleral flap is excised. If the leakage is abundant the scleral flap is repositioned and not sutured because at this point the anterior chamber is formed and there is no need to protect the opening. The risk of postoperative flat chamber is minimized because it is an external non-penetrating procedure.

7. The conjunctival flap is sutured with a running nylon 9-0, taking care to identify the conjunctival borders and avoid suturing to Tenon capsule.

We have used this procedure to treat all types of secondary and refractory glaucomas including cases with neovascular glaucoma where the only options are: Cyclodestructive procedures, retrobulbar alcohol or enucleation

We believe that this new procedure is a simple way to treat difficult cases of refractory glaucomas with a final satisfactory intraocular pressure control. The introduction of a diamond drill (described by us in HIGHLIGHTS OF OPHTHALMOLOGY Bimonthly Letter, 1993 and illustrated in chapter 21 of this Volume) to facilitate the slow dissection of scleral layers, until a permanent flow of aqueous is achieved, facilitates the technique for all ophthalmic surgeons. The use of Mitomycin C at low concentration of 0.08 minimizes the complications attributed to this drug even if it results in an avascularized conjunctival bleb. (World Atlas Series of Ophthalmic Surgery of HIGHLIGHTS, Vol I, 1993).

Our results are better when compared with those obtained with the implantation of a Seton or any other surgical approach for this type of glaucoma. We think this simple technique should be tried once or twice before attempting to do any destructive or complicated procedure.

We have not done a double blind to compare ab-externo posterior trabeculectomy with other glaucoma filtering surgical techniques because we think this procedure guarantees faster recovery and longer survival.

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Chapter 42
THE ROLE OF CYCLOPHOTOABLATION (OR CYCLOPHOTOCOAGULATION)

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The indications for this operation are essentially the same as those for cyclocryotherapy, namely, patients who have failed with maximal medical therapy as well as with one or two filtering procedures, or in eyes with limited visual potential or for patients who are a high risk for incisional surgery. Aphakic glaucoma is the most common indication. This is essentially a ciliary destructive procedure. Whereas in cyclocryotherapy the entire wall of the eye has to be frozen to reach the anterior ciliary processes (Fig. 1), the Nd:YAG or semiconductor diode laser energy can be focused primarily on the ciliary processes destroying them as well as the associated vasculature without seriously affecting the traversed tissues (Fig. 2).

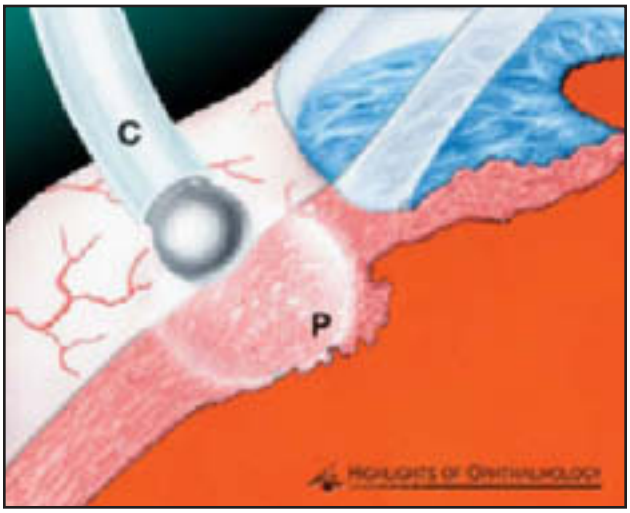


Fig. 1: Differences Between Cyclocryotherapy and Cyclophotoablation

In cyclocryotherapy a cryoprobe (C) is used to destroy tissue on the ciliary processes (P). The entire wall of the eye has to be frozen to reach the anterior ciliary processes. Consequently, the entire wall of the eye is damaged. With cyclophotoablation, patients do not experience the degrees of transient pressure rise, inflammatory response or pain that they feel with cyclocryotherapy.

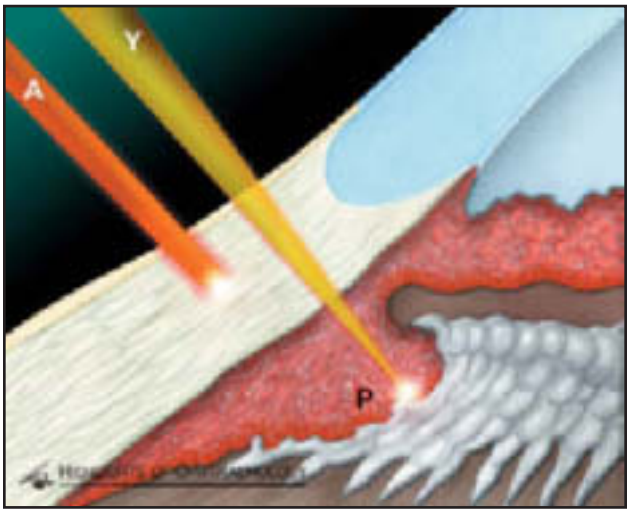


Fig. 2: Differences Between Cyclocryotherapy and Cyclophotoablation

In cyclophotoablation the thermal-mode, non-Q-Switch Neodymium YAG laser (Y) can be focused primarily on the ciliary processes (P). This allows the laser energy to concentrate only on the ciliary processes (P) without seriously affecting the traversed tissues. Argon laser (A) is not recommended because it can only traverse one-sixth the tissue depth that the YAG laser can traverse. Cyclophotoablation may be equal to or slightly better than cyclocryotherapy in terms of pressure reduction.

Bruce Shields and co-workers have been using transscleral cyclo- photoablation with the Nd: YAG laser, and they have been encouraged by their results in over 500 cases, followed for 6 months or more.

Prof. Rosario Brancato in Milan, Italy, is the pioneer on the use of high power, solid state **diode** laser to perform trans-scleral cyclophotocoagulation for uncontrolled glaucoma. His results are better than with the Nd:YAG laser.

Advantages

Shields has found that trans-scleral photoablation seems to have distinct **advantages** over cyclocryotherapy in at least three areas. With cyclophotoablation, patients do not experience the degrees of transient pressure rise, inflammatory response, or pain that patients feel with cyclocryotherapy.

Cyclophotoablation may be equal to or slightly better than cyclocryotherapy, in terms of pressure reduction. Shields and co-workers have been able to control the pressure with one treatment in 60% of their patients. By adding one, two, or as many as five more treatments, they have been able to control the pressure in 95% of these eyes. In a more recent prospective study, randomizing patients to Nd:YAG or diode cyclophotocoagulation, Shields and co-workers found the two procedures to be comparable in efficacy and safety.

The differences between cyclocryotherapy and trans-scleral cyclophotocoagulation (or ablation) are shown in Figs. 1 and 2.

Disadvantages

The **disadvantage** of this treatment, however, is that as many as half of these patients have had some degree of visual acuity reduction. The procedure itself is not always responsible. Diminished vision has sometimes resulted from clouding of the cornea, especially in patients who had previous penetrating keratoplasty. Some loss has also resulted from progression of diabetic retinopathy or already present macular degeneration. Another disadvantage is that the incidence of **sympathetic ophthalmia** after contact and non-contact neodymium:YAG cyclotherapy is high compared with other ocular procedures.

In those cases of vision reduction not attributable to other causes, it is probably due to some degree of cystoid macular edema caused by the laser-induced inflammatory reaction.

Problems in these already damaged eyes also occur with other approaches like the setons and filtering surgery. Until we have definitive evidence of which procedure is the one of choice, the glaucoma surgeon will do best to select the operation that is most effective in his or her hands.

In cases of **chronic angle closure**, or angle closure by synechiae, miotics do not work and trabeculoplasty is not possible. If medical treatment fails, we must turn to a surgical procedure. This could be a filtration with 5-FU or mitomycin or a seton; cyclophotocoagulation, however, is a good choice.

Surgical Technique and Equipment Needed

The standard Nd:YAG laser used for posterior capsulotomy or for iridectomy is not capable of performing transscleral cyclophotocoagulation.

There are several methods and instrumentation used for cyclophotocoagulation. **One** is to perform the procedure with **slit lamp delivery**, as used by **Bruce Shields**. A **second** method is the one introduced by **Prof. Rosario Brancato** delivering the 1064 nm emitted by the Nd:YAG laser through the trans-scleral route using a **contact probe** placed on the conjunctiva 1 - 1.5 mm behind the corneoscleral limbus, obtaining a selective cyclodestruction. **Shields** uses non contact free-running Nd:YAG laser trans-scleral technique (focalizing through a slit lamp the laser beam 1.5 mm behind the limbus), and are able to obtain the same effect.

Shields points out that a laser must have three basic features to perform this procedure with slit lamp delivery. First, there must be the capability



Fig. 3: Area of Destruction of Ciliary Body Following Transscleral Nd:YAG Cyclophotoablation

This view of the internal surface of the ciliary body shows the area of destruction to be grayish-white elevations (circled area). The diameter of the lesions is approximately the width of 2-3 ciliary processes.

for an offset between the helium-neon aiming beam and the therapeutic beam so that when the helium-neon beam is aimed on the conjunctiva, the YAG laser beam can aim deeper into the tissues toward the level of the ciliary body (Fig. 3). Second, much higher energy levels are needed for transscleral cyclophotocoagulation than for capsulotomy or iridectomy. This procedure requires in the range of 4 to 8 joules, or 4,000 to 8,000 milijoules. Third, the procedure must be performed in a thermal or coagulative mode. Unlike the Q-switch mode used for capsulotomy, which lasts 12 nanoseconds, the thermal mode is of longer duration, 20 milliseconds, or 0.02 seconds.

Brancato in Italy has described two methods. One is trans-scleral cyclophotocoagulation with a contact probe rather than the slit lamp. With a fiber-optic contact probe delivery system, this instrument works in a continuous-wave mode so that the duration of the laser effect is much longer. The duration can range from 50 milliseconds to 1 or 2 seconds; most surgeons use a duration of 500 to 700 milliseconds.

Brancato has also described the use of a third method for trans-scleral cyclophotocoagulation. The availability of high power coherent light emitting diode lasers (CLED) has allowed the use of a solid state laser source in several clinical ophthalmic applications, e.g. transpupillary or endophotocoagulation, trabeculoplasty, iridectomy and transscleral cyclophotocoagulation.

Brancato has shown that the **diode laser** provides more effective results than other lasers (Nd:YAG) when performing **transscleral cyclophotocoagulation** for uncontrolled glaucoma. The laser radiation is delivered through a fiber optic, directly in contact with the sclera one (1) mm from the corneal limbus.

The **diode laser** is a small, compact, solid state and practical laser. It does not require the continual maintenance necessary with gas ion lasers, such as the Argon, Krypton and Dye lasers, which are very delicate machines. The Diode laser does not need to be cooled with water; it can be operated with batteries, so it does not consume energy like the Argon or the Krypton lasers. Finally, the cost of the Diode laser will decrease in the future. The Diode laser provides the first application of solid state laser technology for photocoagulation in Ophthalmology. Although Shields found comparable results with the Nd:YAG and diode lasers, he now uses the latter instrument for the reasons noted above.

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